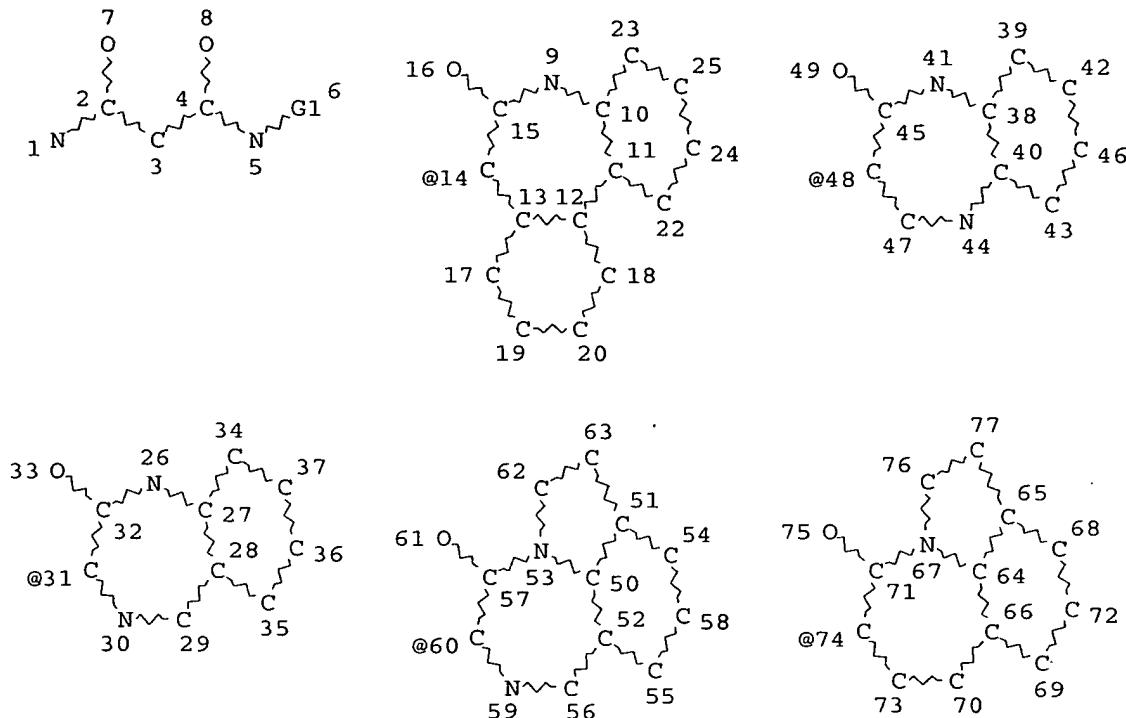
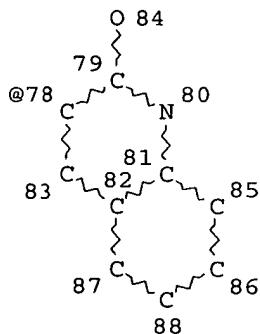


=> d que stat 122
L3 (1) SEA FILE=HCAPLUS ABB=ON PLU=ON US2004-767784/APPS
L4 SEL PLU=ON L3 1- RN : 359 TERMS
L5 359 SEA FILE=REGISTRY ABB=ON PLU=ON L4
L6 STR



Page 1-A



Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 8
CONNECT IS E1 RC AT 16
CONNECT IS E1 RC AT 33
CONNECT IS E1 RC AT 49
CONNECT IS E1 RC AT 61
CONNECT IS E1 RC AT 75
CONNECT IS E1 RC AT 84
DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 87

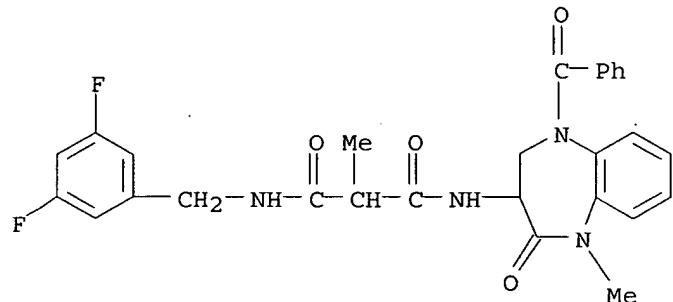
STEREO ATTRIBUTES: NONE

L7	212 SEA FILE=REGISTRY SSS FUL L6
L8	89 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND L7
L21	28 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND F=2
L22	1 SEA FILE=REGISTRY ABB=ON PLU=ON L21 AND C28H26F2N4O4/MF

=> d ide l22

YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y) /N:y

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
 RN 741672-69-5 REGISTRY
 ED Entered STN: 09 Sep 2004
 CN Propanediamide, N-(5-benzoyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl)-N'-(3,5-difluorophenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C28 H26 F2 N4 O4
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

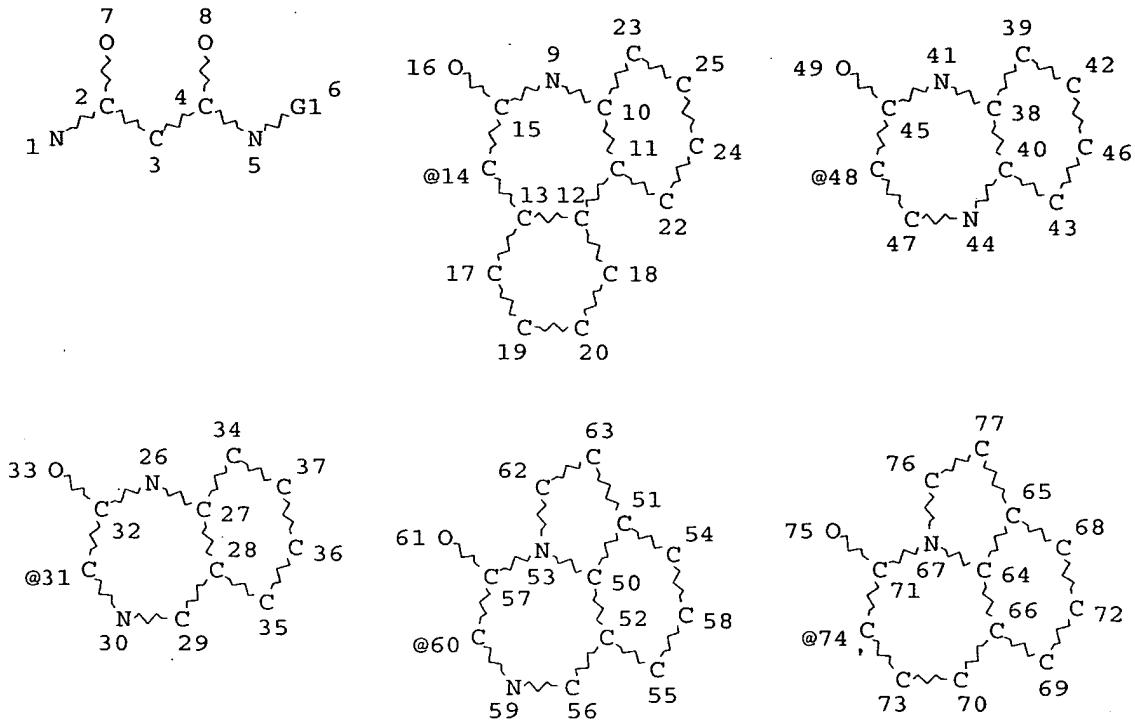
1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file stnguide

FILE 'STNGUIDE' ENTERED AT 10:14:34 ON 01 AUG 2006
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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Jul 28, 2006 (20060728/UP).

=> => d que stat 17
L6 STR



RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 87

STEREO ATTRIBUTES: NONE
L7 212 SEA FILE=REGISTRY SSS FUL L6

100.0% PROCESSED 575 ITERATIONS
SEARCH TIME: 00.00.01

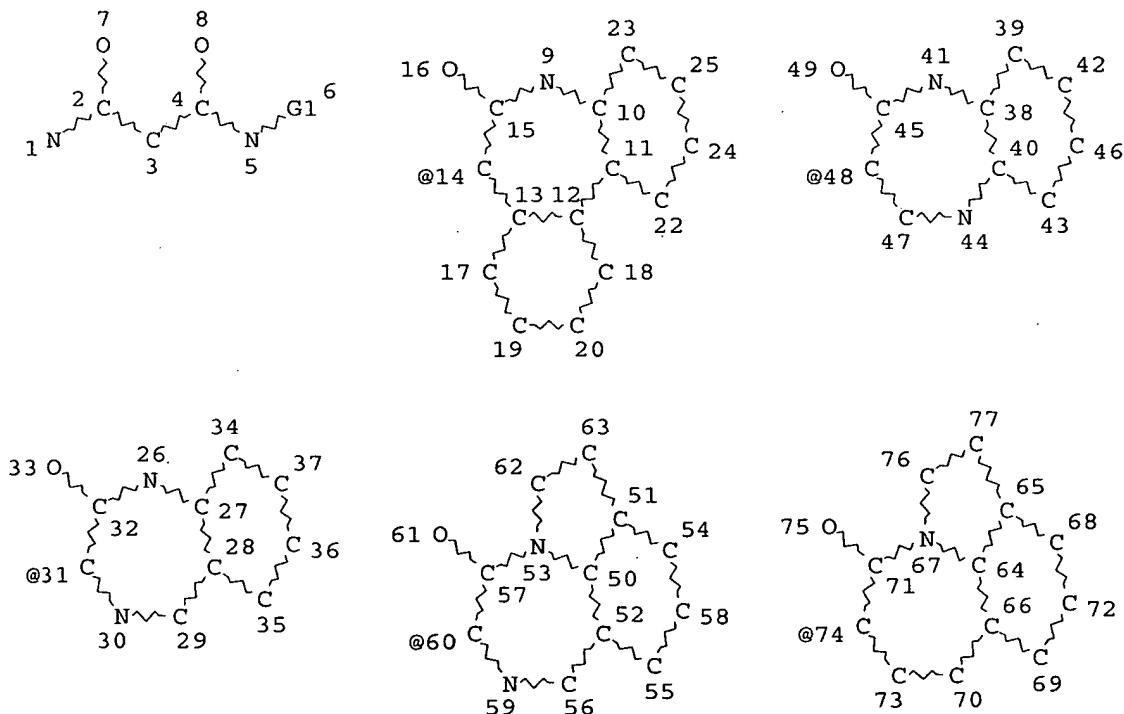
212 ANSWERS

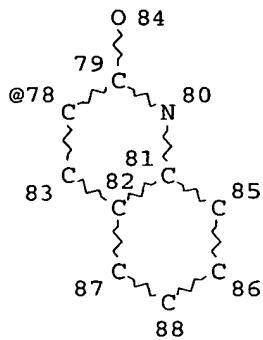
=> d que nos 19
L6 STR
L7 212 SEA FILE=REGISTRY SSS FUL L6
L9 ANALYZE PLU=ON L7 1- LC : 3 TERMS

=> d 19 1-3
L9 ANALYZE L7 1- LC : 3 TERMS

TERM #	# OCC	# DOC	% DOC	LC
1	212	212	100.00	CA
2	212	212	100.00	CAPLUS
3	212	212	100.00	USPATFULL
***** END OF L9 ***				

=> d que stat 123
L6 STR





Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 7
 CONNECT IS E1 RC AT 8
 CONNECT IS E1 RC AT 16
 CONNECT IS E1 RC AT 33
 CONNECT IS E1 RC AT 49
 CONNECT IS E1 RC AT 61
 CONNECT IS E1 RC AT 75
 CONNECT IS E1 RC AT 84
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 87

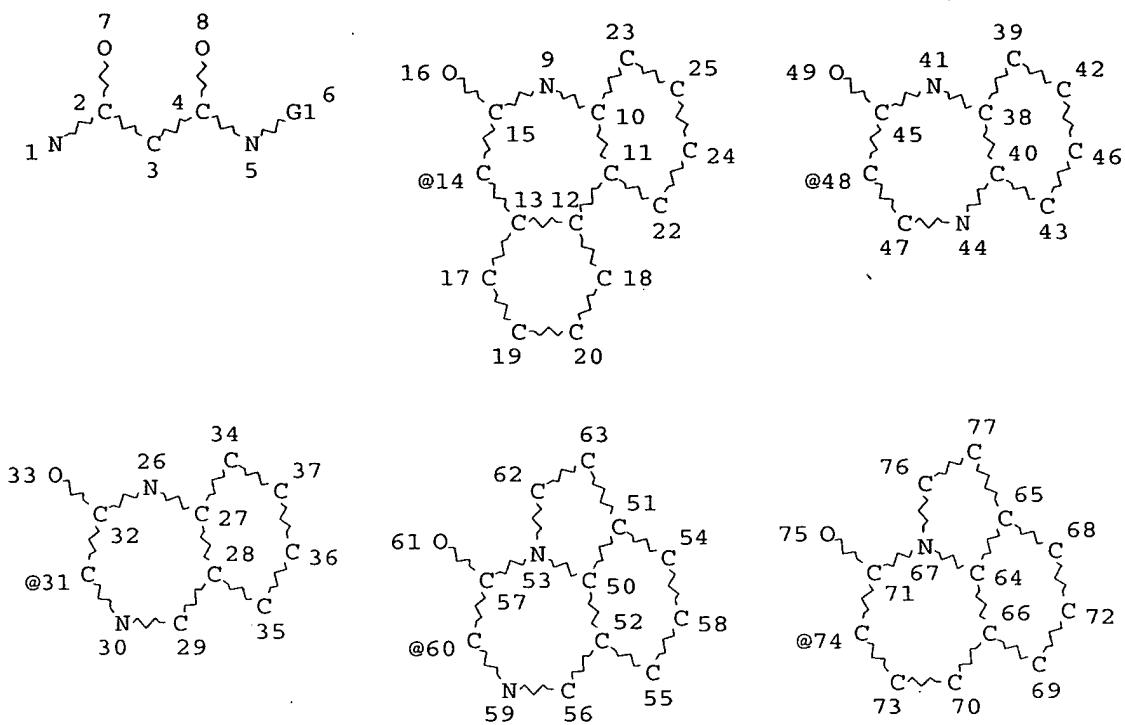
STEREO ATTRIBUTES: NONE

L23 0 SEA FILE=BEILSTEIN SSS FUL L6

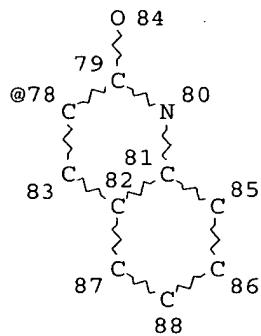
100.0% PROCESSED 31 ITERATIONS
 SEARCH TIME: 00.00.02

0 ANSWERS

=> d que stat 136
 L6 STR



Page 1-A



Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

```

CONNECT IS E1  RC AT    7
CONNECT IS E1  RC AT    8
CONNECT IS E1  RC AT   16
CONNECT IS E1  RC AT   33
CONNECT IS E1  RC AT   49
CONNECT IS E1  RC AT   61
CONNECT IS E1  RC AT   75
CONNECT IS E1  RC AT   84
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

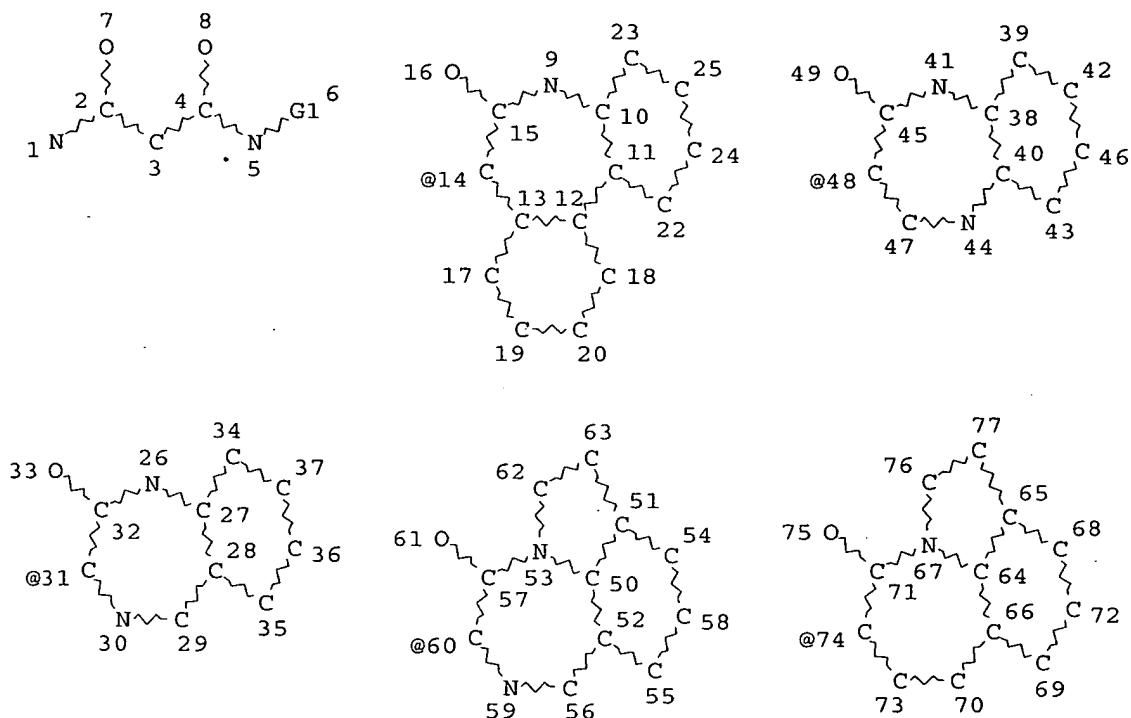
NUMBER OF NODES IS 87

STEREO ATTRIBUTES: NONE

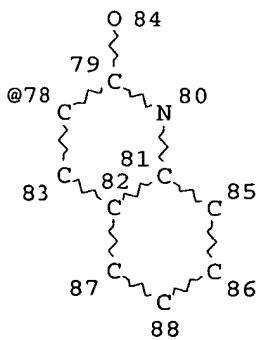
L36 0 SEA FILE=CHEMINFORMRX SSS FUL L6 (0 REACTIONS)

100.0% DONE 3 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.06

=> d his l34

(FILE 'HCAPLUS, USPATFULL, USPAT2' ENTERED AT 10:25:07 ON 01 AUG 2006)
L34 4 S L7=> d que stat l34
L6 STR

Page 1-A



Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 7
 CONNECT IS E1 RC AT 8
 CONNECT IS E1 RC AT 16
 CONNECT IS E1 RC AT 33
 CONNECT IS E1 RC AT 49
 CONNECT IS E1 RC AT 61
 CONNECT IS E1 RC AT 75
 CONNECT IS E1 RC AT 84
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

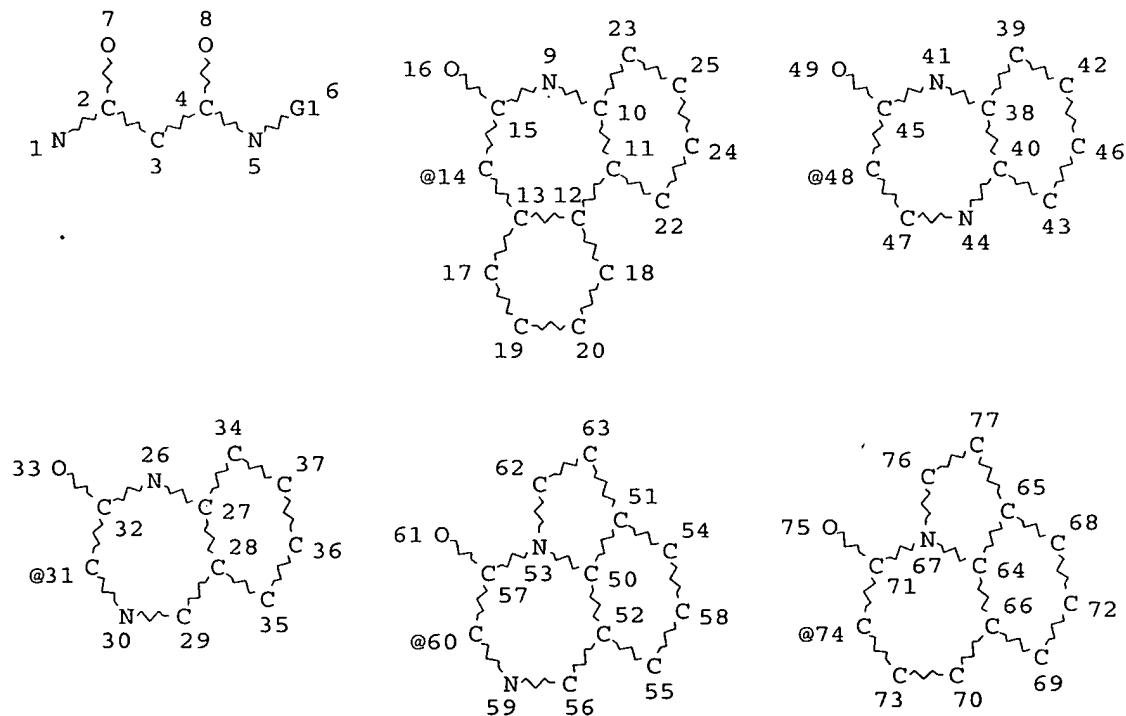
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 87

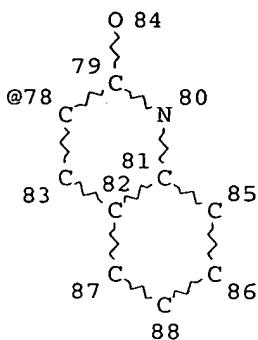
STEREO ATTRIBUTES: NONE

L7 212 SEA FILE=REGISTRY SSS FUL L6
 L34 4 SEA L7

=> d que stat 148
 L6 STR



Page 1-A



Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 7
 CONNECT IS E1 RC AT 8
 CONNECT IS E1 RC AT 16
 CONNECT IS E1 RC AT 33
 CONNECT IS E1 RC AT 49
 CONNECT IS E1 RC AT 61
 CONNECT IS E1 RC AT 75
 CONNECT IS E1 RC AT 84
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 87

STEREO ATTRIBUTES: NONE

L48 82 SEA FILE=WPIX SSS FUL L6

100.0% PROCESSED 88 ITERATIONS
 SEARCH TIME: 00.00.02

82 ANSWERS

=> d his l48-159

(FILE 'WPIX' ENTERED AT 11:32:09 ON 01 AUG 2006)
 L48 82 S L6 FUL
 SAVE TEMP L48 WAR784WPIS/A
 L49 2 S L48/DCR
 SELECT L48 1- SDCN
 L50 2 S E52-E133/DCN
 L51 2 S L49 OR L50
 L52 3816 S L45 OR L46
 L53 18061 S L42 OR L43
 L54 59 S L53 AND L44
 L55 9 S (L52 OR L54) AND (L40/BIX OR L41/BIX)

FILE 'STNGUIDE' ENTERED AT 11:39:04 ON 01 AUG 2006

FILE 'WPIX' ENTERED AT 11:39:48 ON 01 AUG 2006
 L56 29 S (L52 OR L54) AND L25/BIX
 L57 13 S L55-L56 AND (L37/BIX OR ?QUINOLIN?/BIX OR L24/BIX)

L58 13 S L57 OR L51
 L59 12 S L58 NOT (2005-253920)/AN

=> d que nos 159

L6 STR
 L42 QUE ABB=ON PLU=ON (A61K031-47 OR A61K031-4704)/IPC
 L43 QUE ABB=ON PLU=ON (A61K031-55 OR A61K031-551 OR A61K031-5513)/IPC
 L44 QUE ABB=ON PLU=ON (C07C231-00 OR C07C231-02)/IPC
 L45 QUE ABB=ON PLU=ON (D622 (P) J372)/M0,M1,M2,M3,M4,M5,M6
 L46 QUE ABB=ON PLU=ON (D780 (P) J372)/M0,M1,M2,M3,M4,M5,M6
 L48 82 SEA FILE=WPIX SSS FUL L6
 L49 2 SEA FILE=WPIX ABB=ON PLU=ON L48/DCR
 L50 2 SEA FILE=WPIX ABB=ON PLU=ON (RAF7SZ/DCN OR RAF81C/DCN OR
 RAF81D/DCN OR RAF81E/DCN OR RAF81F/DCN OR RAF81G/DCN OR
 RAF81K/DCN OR RAF81L/DCN OR RAF81M/DCN OR RAF81N/DCN OR
 RAF81O/DCN OR RAF81P/DCN OR RAF81Q/DCN OR RAF81R/DCN OR
 RAF81S/DCN OR RAF81T/DCN OR RAF81V/DCN OR RAF81W/DCN OR
 RAF81X/DCN OR RAF81Y/DCN OR RAF81Z/DCN OR RAF820/DCN OR
 RAF821/DCN OR RAF822/DCN OR RAF823/DCN OR RAF824/DCN OR
 RAF825/DCN OR RAF826/DCN OR RAF827/DCN OR RAH9NA/DCN OR
 RAH9NB/DCN OR RAH9ND/DCN OR RAH9NE/DCN OR RAH9NG/DCN OR
 RAH9NH/DCN OR RAH9NI/DCN OR RAH9NK/DCN OR RAH9NM/DCN OR
 RAH9NO/DCN OR RAH9NP/DCN OR RAH9NR/DCN OR RAH9NS/DCN OR
 RAH9NT/DCN OR RAH9NV/DCN OR RAH9NW/DCN OR RAH9NY/DCN OR
 RAH9NZ/DCN OR RAH9N6/DCN OR RAH9N8/DCN OR RAH9N9/DCN OR
 RAH9OA/DCN OR RAH9OB/DCN OR RAH9OD/DCN OR RAH9OE/DCN OR
 RAH9OG/DCN OR RAH9OH/DCN OR RAH9OI/DCN OR RAH9OK/DCN OR
 RAH9OM/DCN OR RAH9ON/DCN OR RAH9OP/DCN OR RAH9OQ/DCN OR
 RAH9OR/DCN OR RAH9OT/DCN OR RAH9OV/DCN OR RAH9OX/DCN OR
 RAH9OY/DCN OR RAH9OZ/DCN OR RAH9O1/DCN OR RAH9O3/DCN OR
 RAH9O5/DCN OR RAH9O6/DCN OR RAH9O8/DCN OR RAH9PB/DCN OR
 RAH9PC/DCN OR RAH9PD/DCN OR RAH9PF/DCN OR RAH9P1/DCN OR
 RAH9P3/DCN OR RAH9P7/DCN OR RAH9P8/DCN OR RAH9P9/DCN)
 L51 2 SEA FILE=WPIX ABB=ON PLU=ON L49 OR L50
 L52 3816 SEA FILE=WPIX ABB=ON PLU=ON L45 OR L46
 L53 18061 SEA FILE=WPIX ABB=ON PLU=ON L42 OR L43
 L54 59 SEA FILE=WPIX ABB=ON PLU=ON L53 AND L44
 L55 9 SEA FILE=WPIX ABB=ON PLU=ON ((L52 OR L54) AND ((?MALONAMID?/BIX
 OR ?MALONODIAMID?/BIX OR ?PROPANEDIAMID?/BIX OR ((?MALON/BIX
 OR ?PROPAN?/BIX OR ?PROPYL?/BIX OR ?PROPANYL?/BIX) (1A) (DIAMID?/
 BIX OR (DI/BIX(W)AMID?/BIX)))) OR (?MALONIC/BIX (2A) (AMID?/BIX
 OR DIAMID?/BIX)))
 L56 29 SEA FILE=WPIX ABB=ON PLU=ON (L52 OR L54) AND (?MALON?/BIX)
 L57 13 SEA FILE=WPIX ABB=ON PLU=ON (L55 OR L56) AND ((?HYDROQUINOLIN?
 /BIX OR TETRAHYDROQUINOLIN?/BIX OR ((HYDRO/BIX OR TETRAHYDRO/B
 IX) (2A) QUINOLIN?/BIX)) OR ?QUINOLIN?/BIX OR (?AZEPIN?/BIX))
 L58 13 SEA FILE=WPIX ABB=ON PLU=ON L57 OR L51
 L59 12 SEA FILE=WPIX ABB=ON PLU=ON L58 NOT (2005-253920)/AN

=> d que stat 182

L19 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY
 <2004 OR REVIEW/DT
 L24 QUE ABB=ON PLU=ON ?AZEPIN?
 L25 QUE ABB=ON PLU=ON ?MALON?
 L37 QUE ABB=ON PLU=ON ?HYDROQUINOLIN? OR TETRAHYDROQUINOLI
 N? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
 L80 18 SEA FILE=MEDLINE ABB=ON PLU=ON (L24 OR L37) (7A)L25
 L81 18 SEA FILE=MEDLINE ABB=ON PLU=ON L80 AND L19

L82 4 SEA FILE=MEDLINE ABB=ON PLU=ON L81 NOT (?CHROMAT? OR HPLC OR KINETIC? OR BLISTER OR IRRITANT)/TI

=> d que stat 189

L19 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY <2004 OR REVIEW/DT
 L24 QUE ABB=ON PLU=ON ?AZEPIN?
 L25 QUE ABB=ON PLU=ON ?MALON?
 L37 QUE ABB=ON PLU=ON ?HYDROQUINOLIN? OR TETRAHYDROQUINOLIN? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
 L40 QUE ABB=ON PLU=ON ?MALONAMID? OR ?MALONODIAMID? OR ?PROPANEDIAMID? OR ((?MALON OR ?PROPAN? OR ?PROPYL? OR ?PROPNYL?) (1A) (DIAMID? OR (DI(W)AMID?)))
 L41 QUE ABB=ON PLU=ON ?MALONIC (2A) (AMID? OR DIAMID?)
 L87 26 SEA FILE=EMBASE ABB=ON PLU=ON (L24 OR L37) (7A) (L25 OR L40 OR L41)
 L88 26 SEA FILE=EMBASE ABB=ON PLU=ON L87 AND L19
 L89 5 SEA FILE=EMBASE ABB=ON PLU=ON L88 NOT (CHROMATOG? OR HPLC OR KINETIC? OR BLISTER OR IRRITANT? OR MONITOR?)/TI

=> d his 197

(FILE 'BIOSIS, PASCAL, JICST-EPLUS, JAPIO, LIFESCI, BIOENG, CABA, BIOTECHNO, BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI, DISSABS' ENTERED AT 12:29:41 ON 01 AUG 2006)
 L97 7 S L96 NOT (CHROMATOG? OR HPLC)/TI
 SAVE TEMP L97 WAR784MUL1B/A

FILE 'STNGUIDE' ENTERED AT 12:43:37 ON 01 AUG 2006

=> d que stat 197

L24 QUE ABB=ON PLU=ON ?AZEPIN?
 L37 QUE ABB=ON PLU=ON ?HYDROQUINOLIN? OR TETRAHYDROQUINOLIN? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
 L40 QUE ABB=ON PLU=ON ?MALONAMID? OR ?MALONODIAMID? OR ?PROPANEDIAMID? OR ((?MALON OR ?PROPAN? OR ?PROPYL? OR ?PROPNYL?) (1A) (DIAMID? OR (DI(W)AMID?)))
 L41 QUE ABB=ON PLU=ON ?MALONIC (2A) (AMID? OR DIAMID?)
 L94 308 SEA (L24 OR ?DIAZEPIN? OR L37) (7A) (L37 OR L40 OR L41)
 L96 25 SEA L94 AND (L40 OR L41)
 L97 7 SEA L96 NOT (CHROMATOG? OR HPLC)/TI

=> dup rem 134 159 182 189 197

FILE 'HCAPLUS' ENTERED AT 12:47:00 ON 01 AUG 2006
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FILE 'EMBASE' ENTERED AT 12:47:00 ON 01 AUG 2006

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PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L59
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L89
PROCESSING COMPLETED FOR L97

L98 25 DUP REM L34 L59 L82 L89 L97 (7 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE HCAPLUS
ANSWER '3' FROM FILE USPATFULL
ANSWERS '4-13' FROM FILE WPIX
ANSWERS '14-17' FROM FILE MEDLINE
ANSWERS '18-20' FROM FILE EMBASE
ANSWERS '21-25' FROM FILE BIOSIS

=> file stnguide

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jul 28, 2006 (20060728/UP).

=> file stnguide

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jul 28, 2006 (20060728/UP).

=> d ibib ed ab hitstr retable 1-2
 YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, WPIX, MEDLINE, EMBASE,
 BIOSIS' - CONTINUE? (Y)/N:y

L98 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2005:220131 HCAPLUS
 DOCUMENT NUMBER: 142:298014
 TITLE: Preparation of dibenzoazepinylmalonamides,
 dibenzoepinylmalonamides,
 benzodiazepinylmalonamides, and related compounds as
 γ -secretase inhibitors for treatment of
 Alzheimer's disease.
 INVENTOR(S): Flohr, Alexander; Galley, Guido; Jakob-Roetne, Roland;
 Kitas, Eric Argirios; Peters, Jens-Uwe; Wostl,
 Wolfgang
 PATENT ASSIGNEE(S): Switz.
 SOURCE: U.S. Pat. Appl. Publ., 59 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005054633	A1	20050310	US 2004-933177	20040902
AU 2004270361	A1	20050317	AU 2004-270361	20040831
CA 2537440	AA	20050317	CA 2004-2537440	20040831
WO 2005023772	A1	20050317	WO 2004-EP9700	20040831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NO 2006001047	A	20060404	NO 2006-1047	20060303
PRIORITY APPLN. INFO.:			EP 2003-19683	A 20030909
			WO 2004-EP9700	W 20040831

OTHER SOURCE(S): MARPAT 142:298014
 ED Entered STN: 13 Mar 2005
 AB Malonamides R1NHCOCR3R4CONHR2 [R1= Q1-Q4; R2 = alkyl, alkynyl, alkylthio,
 alkoxy(alkyl), halo(alkyl), etc.; R3, R4 = H, alkyl, alkoxy, Ph, halo; R5
 = H, alkyl, trifluoromethyl(alkyl), cycloalkyl(alkyl); R6 = H, halo; R7 =
 H, alkyl; R8 = H, alkyl, alkynyl, trifluoromethyl(alkyl),
 cycloalkyl(alkyl), (halo-substituted) phenyl(alkyl); R9 = H, alkyl, CHO,
 alkylcarbonyl, F3CCO, (substituted) PhCO, etc.], were prepared Thus,
 2-methyl-N-(5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-
 yl)malonamic acid (preparation given), cyclopropylmethylamine, and
 2-(2-pyridon-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TPTU)
 were shaken together overnight in DMF to give N-cyclopropylmethyl-2-methyl-
 N'-(5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl)malonamide. The
 latter inhibited γ -secretase with IC50 = 0.09 μ M.
 IT 847925-73-9P 847925-74-0P 847925-75-1P

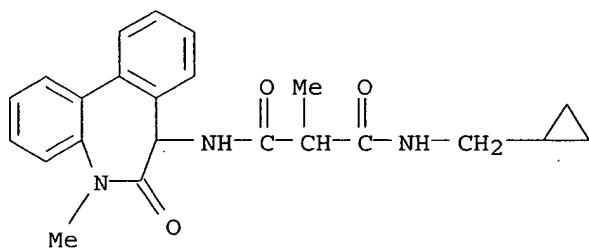
847925-76-2P 847925-77-3P 847925-78-4P
 847925-79-5P 847925-80-8P 847925-81-9P
 847925-83-1P 847925-84-2P 847925-85-3P
 847925-86-4P 847925-87-5P 847925-88-6P
 847925-89-7P 847925-90-0P 847925-91-1P
 847925-92-2P 847925-93-3P 847925-94-4P
 847925-95-5P 847925-96-6P 847925-97-7P
 847925-98-8P 847925-99-9P 847926-00-5P
 847926-01-6P 847926-02-7P 847926-03-8P
 847926-04-9P 847926-05-0P 847926-06-1P
 847926-07-2P 847926-08-3P 847926-09-4P
 847926-10-7P 847926-11-8P 847926-12-9P
 847926-13-0P 847926-15-2P 847926-16-3P
 847926-17-4P 847926-18-5P 847926-19-6P
 847926-20-9P 847926-21-0P 847926-22-1P
 847926-23-2P 847926-24-3P 847926-25-4P
 847926-26-5P 847926-27-6P 847926-28-7P
 847926-29-8P 847926-30-1P 847926-31-2P
 847926-32-3P 847926-33-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of dibenzoazepinylmalonamides, dibenzoepoxymalonamides, benzodiazepinylmalonamides, and related compds. as γ -secretase inhibitors for treatment of Alzheimer's disease)

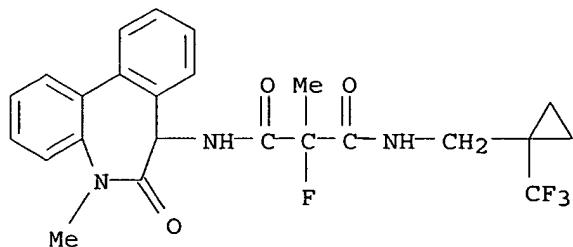
RN 847925-73-9 HCPLUS

CN Propanediamide, N-(cyclopropylmethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



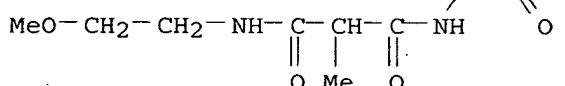
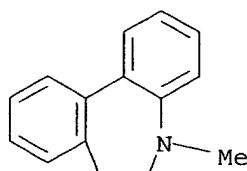
RN 847925-74-0 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-[1-(trifluoromethyl)cyclopropylmethyl]- (9CI) (CA INDEX NAME)



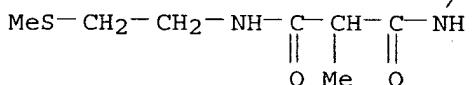
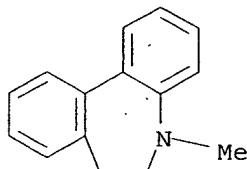
RN 847925-75-1 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-methoxyethyl)-2-methyl- (9CI) (CA INDEX NAME)



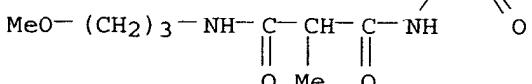
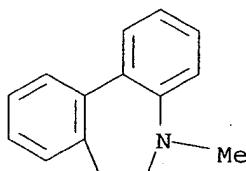
RN 847925-76-2 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2-(methylthio)ethyl)- (9CI) (CA INDEX NAME)



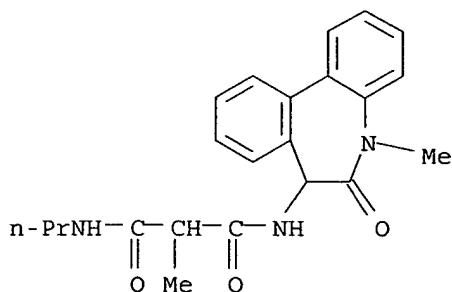
RN 847925-77-3 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(3-methoxypropyl)-2-methyl- (9CI) (CA INDEX NAME)



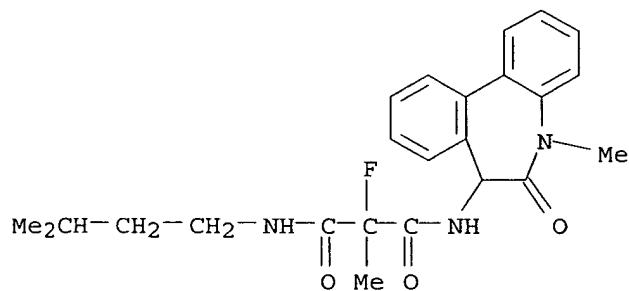
RN 847925-78-4 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-propyl- (9CI) (CA INDEX NAME)



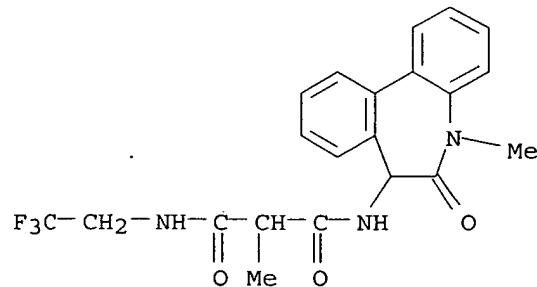
RN 847925-79-5 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(3-methylbutyl)- (9CI) (CA INDEX NAME)



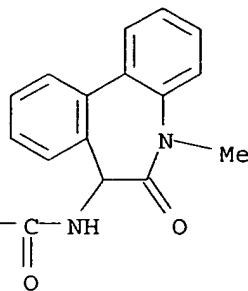
RN 847925-80-8 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)



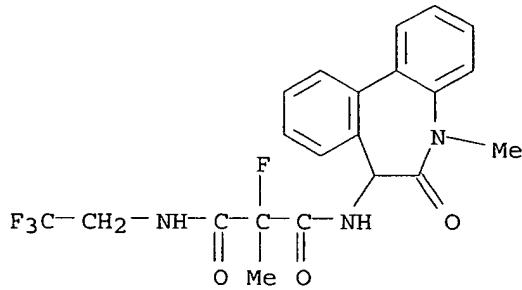
RN 847925-81-9 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



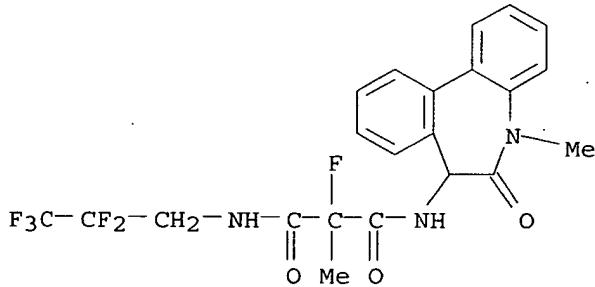
RN 847925-83-1 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)



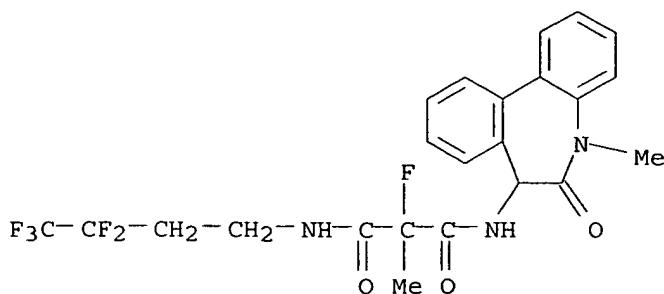
RN 847925-84-2 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



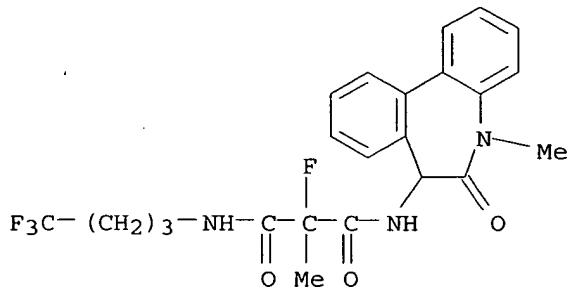
RN 847925-85-3 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)- (9CI) (CA INDEX NAME)



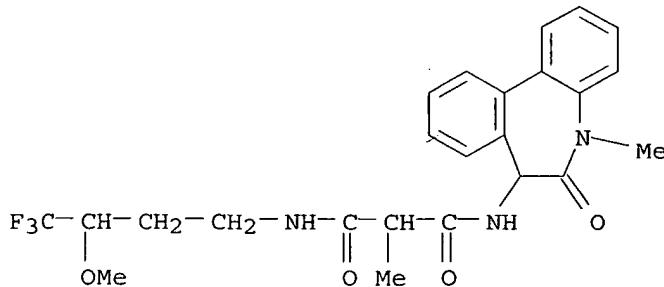
RN 847925-86-4 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(4,4,4-trifluorobutyl) - (9CI) (CA INDEX NAME)



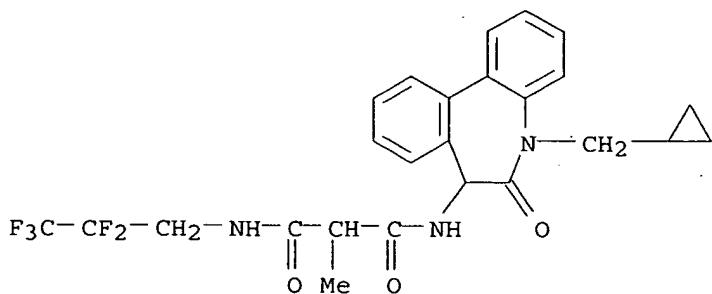
RN 847925-87-5 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(4,4,4-trifluoro-3-methoxybutyl) - (9CI) (CA INDEX NAME)



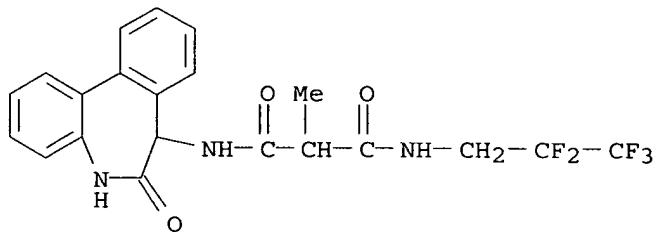
RN 847925-88-6 HCAPLUS

CN Propanediamide, N-[5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl) - (9CI) (CA INDEX NAME)



RN 847925-89-7 HCAPLUS

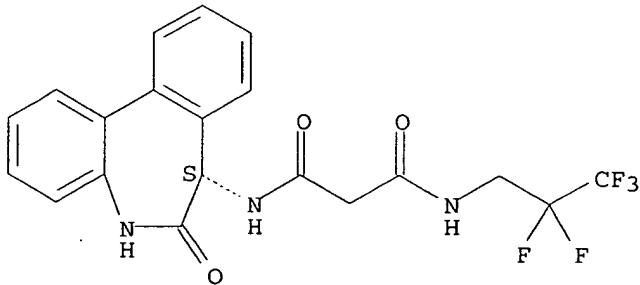
CN Propanediamide, N-(6,7-dihydro-6-oxo-5H-dibenzo[b,d]azepin-7-yl)-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847925-90-0 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

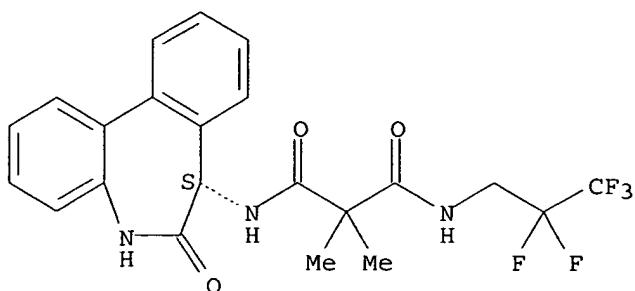
Absolute stereochemistry. Rotation (-).



RN 847925-91-1 HCAPLUS

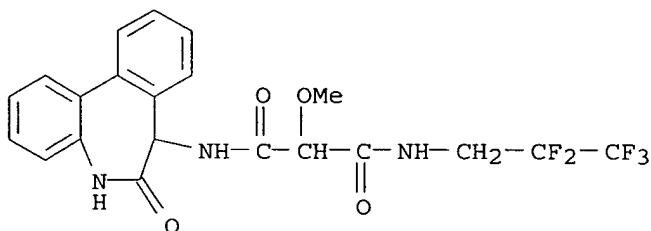
CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenzo[b,d]azepin-7-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 847925-92-2 HCAPLUS

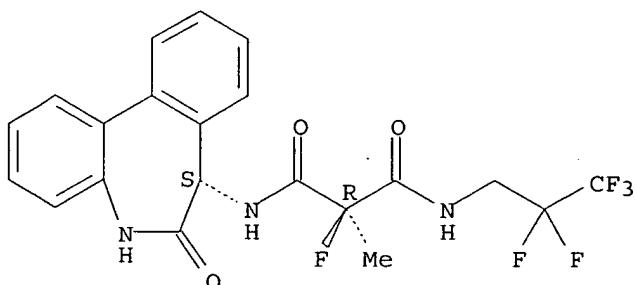
CN Propanediamide, N-(6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methoxy-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847925-93-3 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(2R)-(9CI) (CA INDEX NAME)

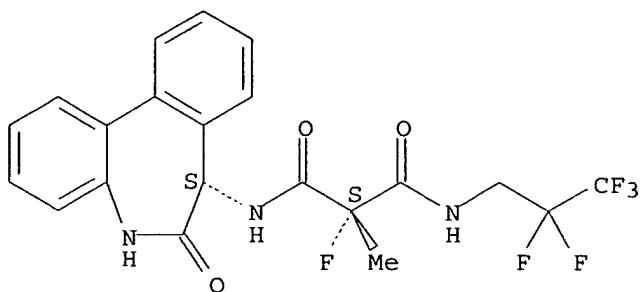
Absolute stereochemistry.



RN 847925-94-4 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(2S)-(9CI) (CA INDEX NAME)

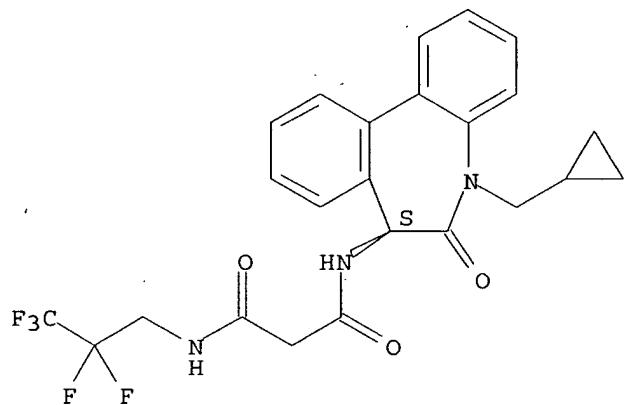
Absolute stereochemistry.



RN 847925-95-5 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

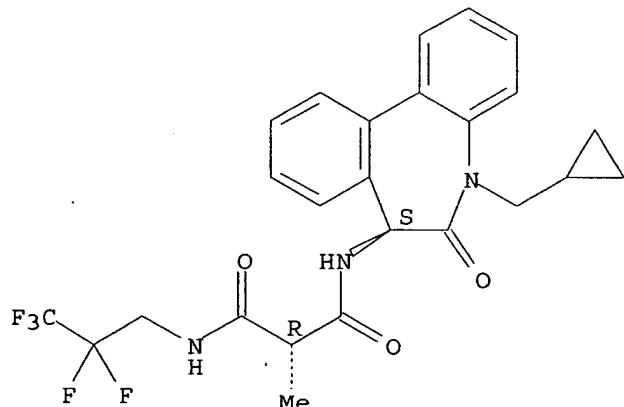
Absolute stereochemistry. Rotation (-).



RN 847925-96-6 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(2R)-(9CI) (CA INDEX NAME)

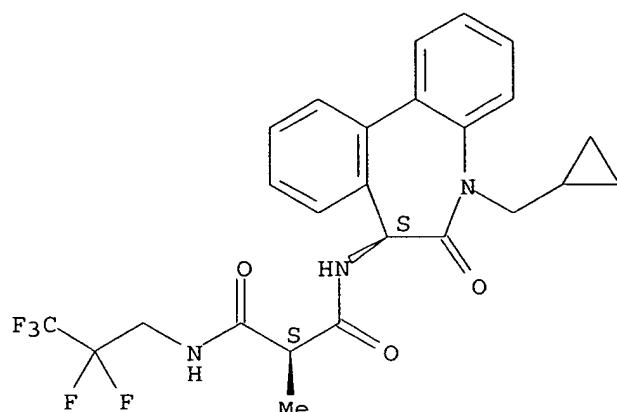
Absolute stereochemistry. Rotation (-).



RN 847925-97-7 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2S) - (9CI) (CA INDEX NAME)

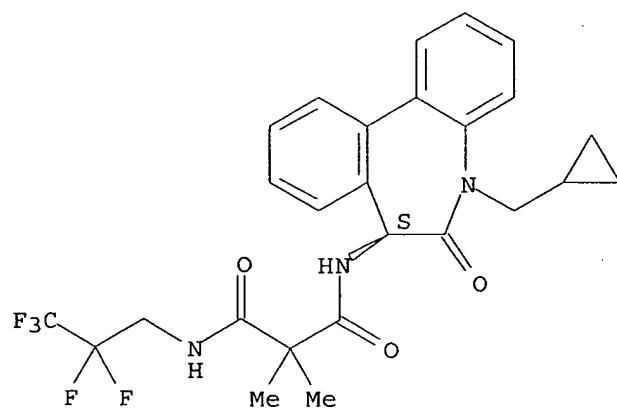
Absolute stereochemistry.



RN 847925-98-8 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

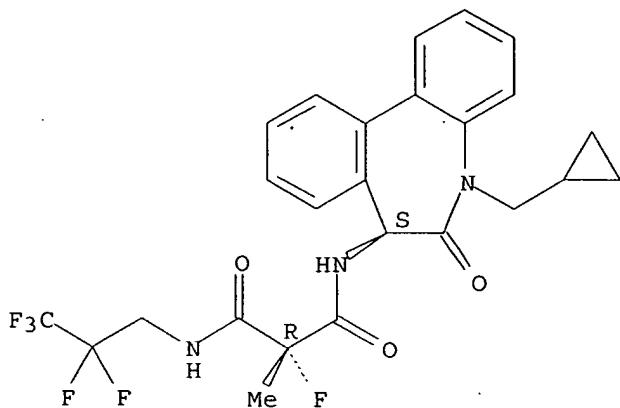
Absolute stereochemistry. Rotation (-).



RN 847925-99-9 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2R) - (9CI) (CA INDEX NAME)

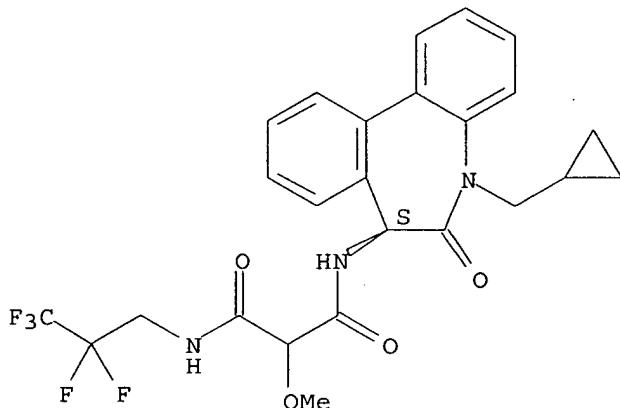
Absolute stereochemistry. Rotation (-).



RN 847926-00-5 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methoxy-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI)
(CA INDEX NAME)

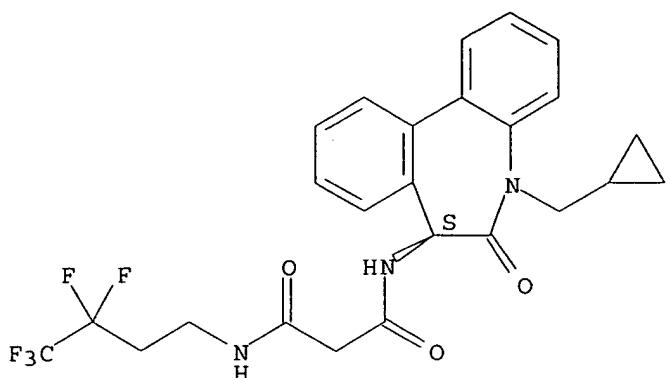
Absolute stereochemistry.



RN 847926-01-6 HCAPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-N'-(3,3,4,4,4-pentafluorobutyl)- (9CI) (CA INDEX NAME)

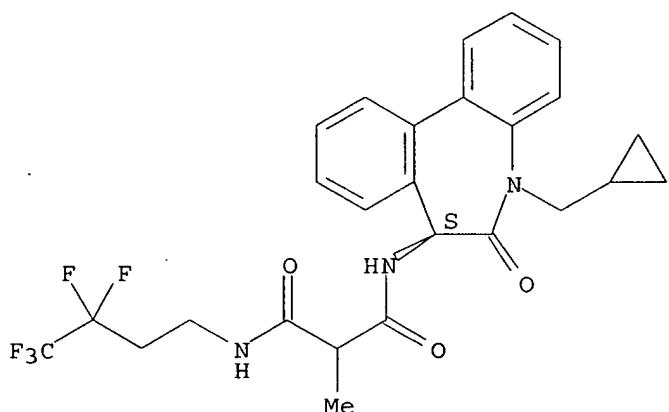
Absolute stereochemistry. Rotation (-).



RN 847926-02-7 HCPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenzo[b,d]azepin-7-yl]-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-(9CI)
(CA INDEX NAME)

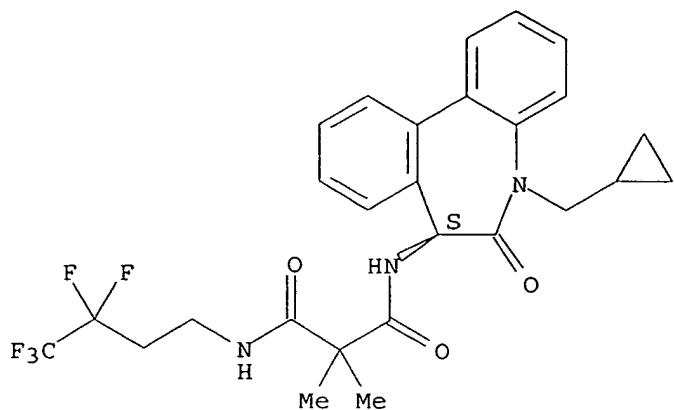
Absolute stereochemistry.



RN 847926-03-8 HCPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenzo[b,d]azepin-7-yl]-2,2-dimethyl-N'-(3,3,4,4,4-pentafluorobutyl)-(9CI)
(CA INDEX NAME)

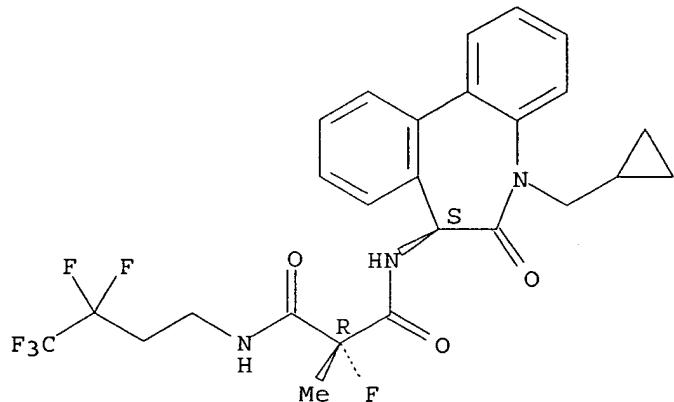
Absolute stereochemistry. Rotation (-).



RN 847926-04-9 HCAPLUS

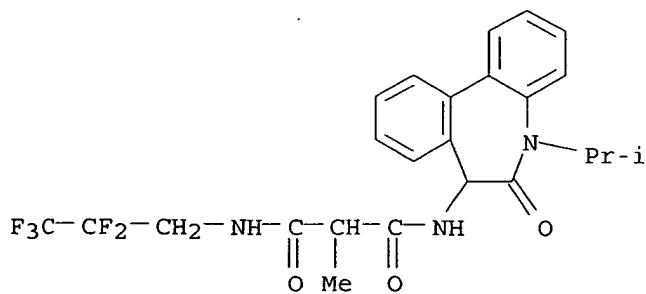
CN Propanediamide, N-[{(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl}-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-(2R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



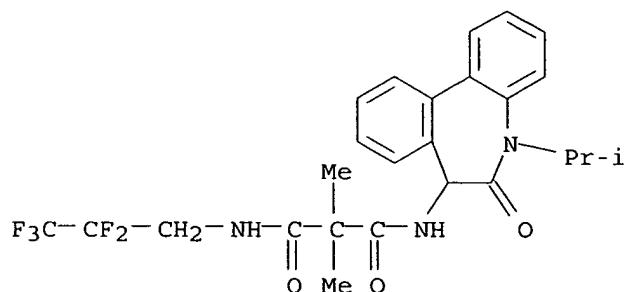
RN 847926-05-0 HCAPLUS

CN Propanediamide, N-[{6,7-dihydro-5-(1-methylethyl)-6-oxo-5H-dibenz[b,d]azepin-7-yl}-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847926-06-1 HCAPLUS

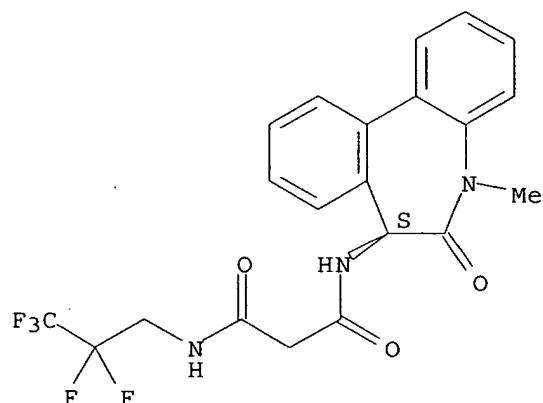
CN Propanediamide, N-[6,7-dihydro-5-(1-methylethyl)-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847926-07-2 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

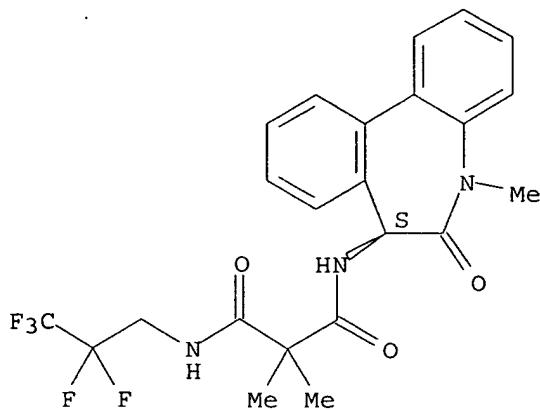
Absolute stereochemistry. Rotation (-).



RN 847926-08-3 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

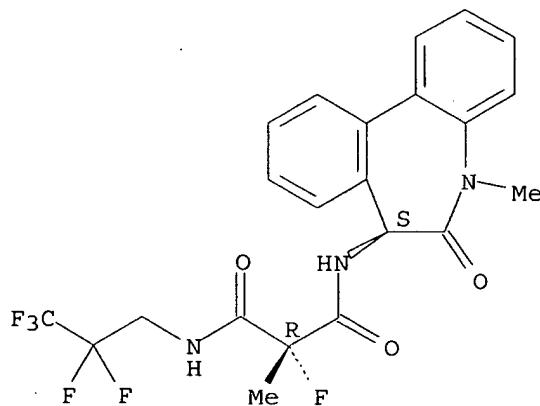
Absolute stereochemistry. Rotation (-).



RN 847926-09-4 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2R)- (9CI) (CA INDEX NAME)

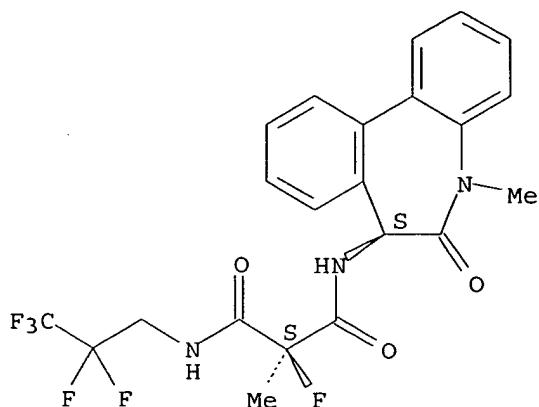
Absolute stereochemistry.



RN 847926-10-7 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2S)- (9CI) (CA INDEX NAME)

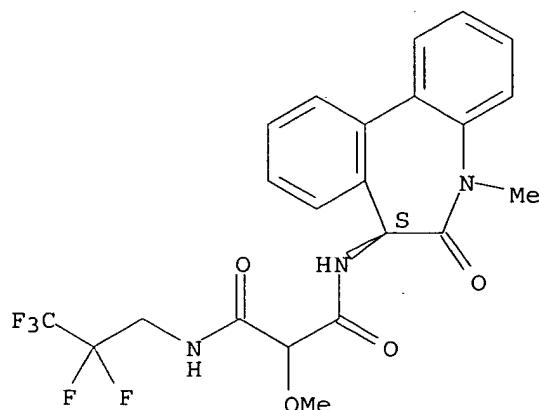
Absolute stereochemistry.



RN 847926-11-8 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methoxy-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

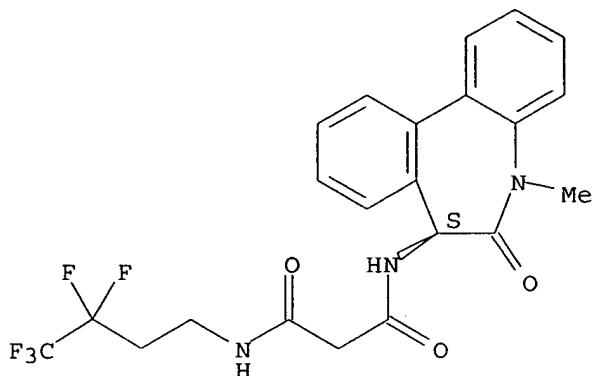
Absolute stereochemistry.



RN 847926-12-9 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-N'-(3,3,4,4,4-pentafluorobutyl)- (9CI) (CA INDEX NAME)

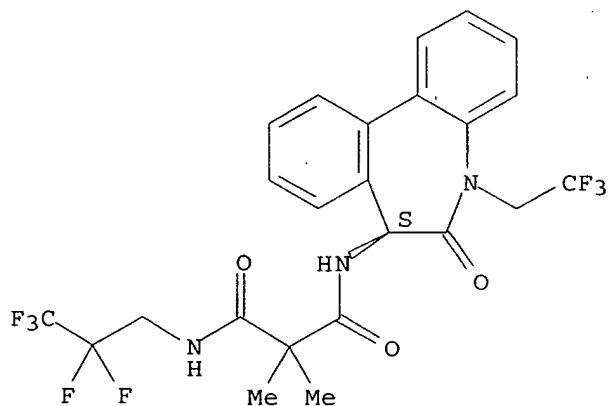
Absolute stereochemistry. Rotation (-).



RN 847926-13-0 HCAPLUS

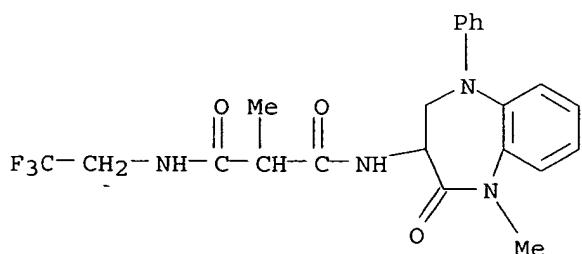
CN Propanediamide, N-[(7S) -6,7-dihydro-6-oxo-5-(2,2,2-trifluoroethyl)-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 847926-15-2 HCAPLUS

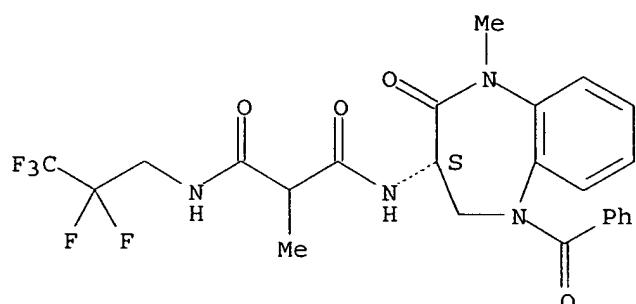
CN Propanediamide, 2-methyl-N-(2,3,4,5-tetrahydro-1-methyl-2-oxo-5-phenyl-1H-1,5-benzodiazepin-3-yl)-N'-(2,2,2-trifluoroethyl)-(9CI) (CA INDEX NAME)



RN 847926-16-3 HCAPLUS

CN Propanediamide, N-[(3S) -5-benzoyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

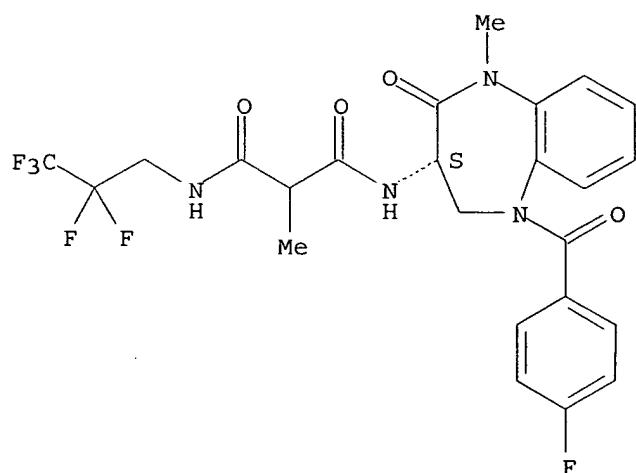
Absolute stereochemistry.



RN 847926-17-4 HCAPLUS

CN Propanediamide, N-[(3S)-5-(4-fluorobenzoyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

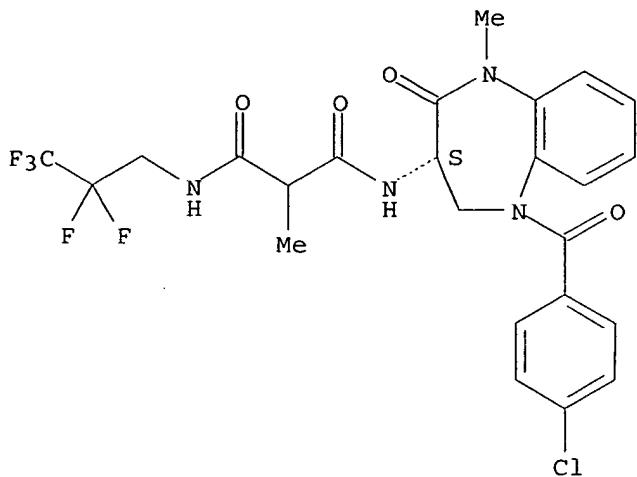
Absolute stereochemistry.



RN 847926-18-5 HCAPLUS

CN Propanediamide, N-[(3S)-5-(4-chlorobenzoyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

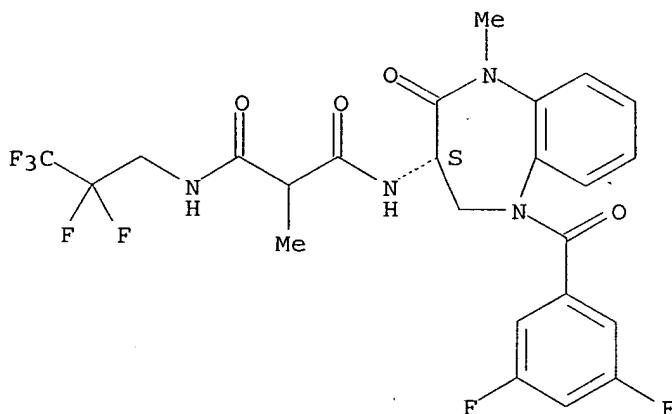
Absolute stereochemistry.



RN 847926-19-6 HCPLUS

CN Propanediamide, N-[(3S)-5-(3,5-difluorobenzoyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

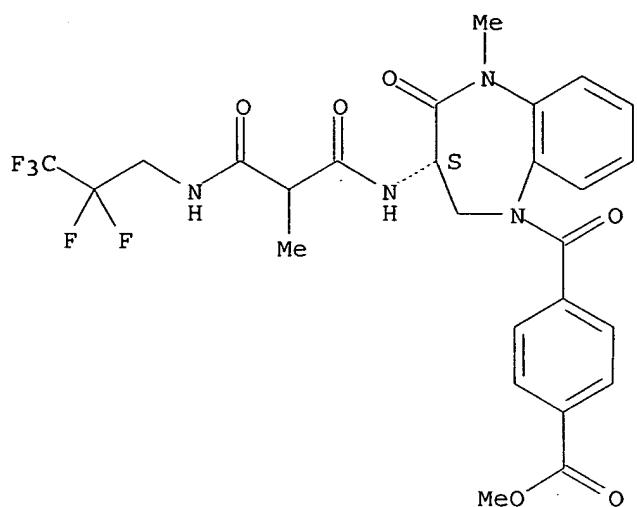
Absolute stereochemistry.



RN 847926-20-9 HCPLUS

CN Benzoic acid, 4-[[[(3S)-2,3,4,5-tetrahydro-5-methyl-3-[[2-methyl-1,3-dioxo-3-[(2,2,3,3,3-pentafluoropropyl)amino]propyl]amino]-4-oxo-1H-1,5-benzodiazepin-1-yl]carbonyl], methyl ester (9CI) (CA INDEX NAME)

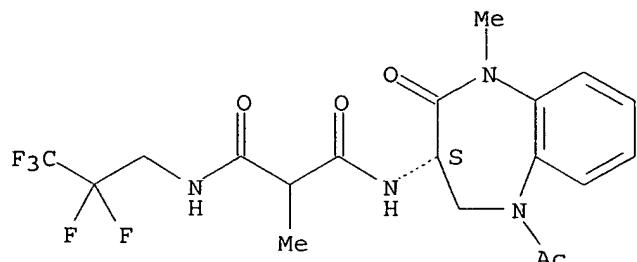
Absolute stereochemistry.



RN 847926-21-0 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

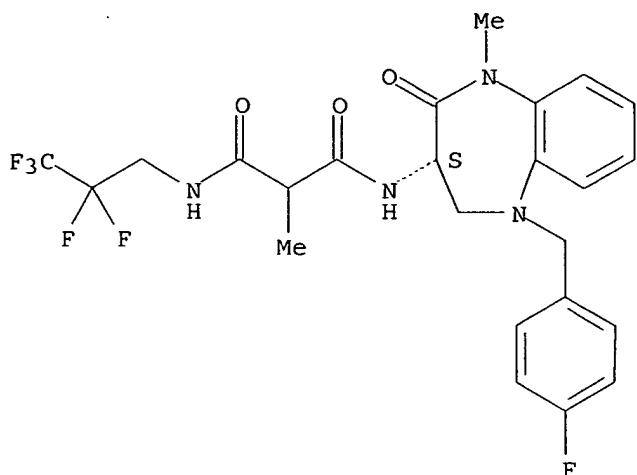
Absolute stereochemistry.



RN 847926-22-1 HCPLUS

CN Propanediamide, N-[(3S)-5-[(4-fluorophenyl)methyl]-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

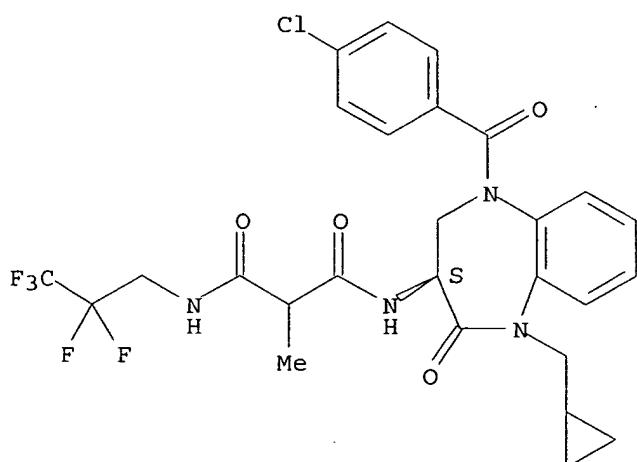
Absolute stereochemistry.



RN 847926-23-2 HCAPLUS

CN Propanediamide, N-[(3S)-5-(4-chlorobenzoyl)-1-(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

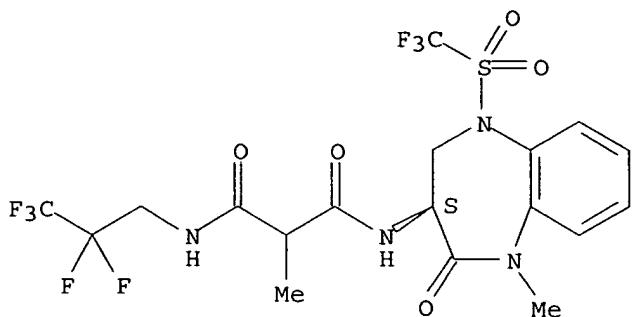
Absolute stereochemistry.



RN 847926-24-3 HCAPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-[2,3,4,5-tetrahydro-1-methyl-2-oxo-5-[(trifluoromethyl)sulfonyl]-1H-1,5-benzodiazepin-3-yl]-(9CI) (CA INDEX NAME)

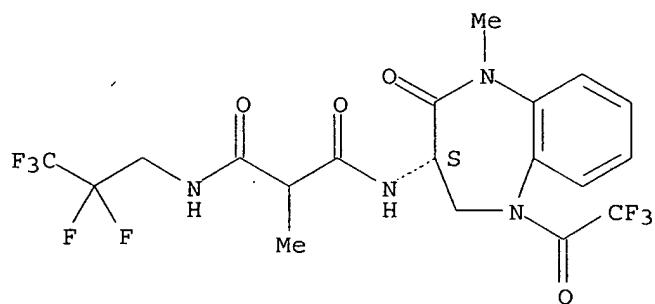
Absolute stereochemistry.



RN 847926-25-4 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-1-methyl-2-oxo-5-(trifluoroacetyl)-1H-1,5-benzodiazepin-3-yl]-(9CI) (CA INDEX NAME)

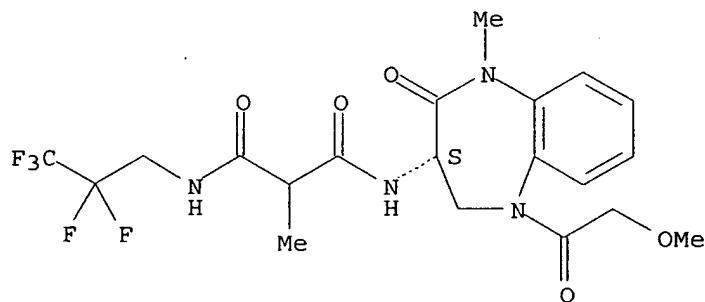
Absolute stereochemistry.



RN 847926-26-5 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-5-(methoxyacetyl)-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-(9CI) (CA INDEX NAME)

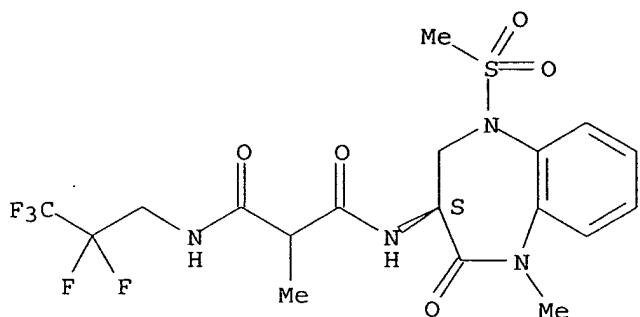
Absolute stereochemistry.



RN 847926-27-6 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-1-methyl-5-(methylsulfonyl)-2-oxo-1H-1,5-benzodiazepin-3-yl]-(9CI) (CA INDEX NAME)

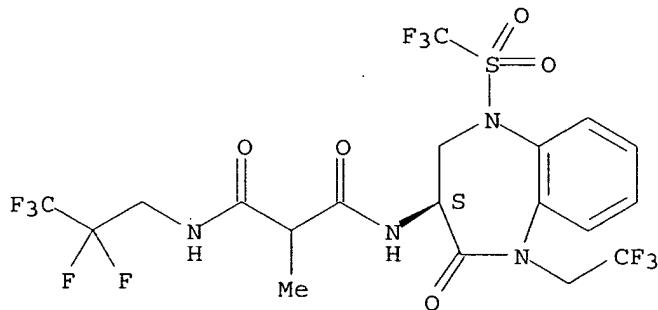
Absolute stereochemistry.



RN 847926-28-7 HCAPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-2-oxo-1-(2,2,2-trifluoroethyl)-5-[(trifluoromethyl)sulfonyl]-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)

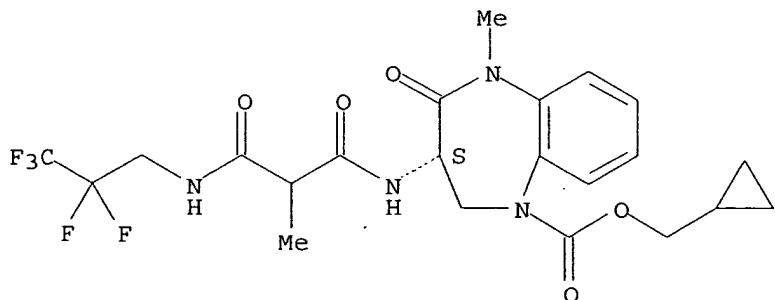
Absolute stereochemistry.



RN 847926-29-8 HCAPLUS

CN 1H-1,5-Benzodiazepine-1-carboxylic acid, 2,3,4,5-tetrahydro-5-methyl-3-[(2-methyl-1,3-dioxo-3-[(2,2,3,3,3-pentafluoropropyl)amino]propyl)amino]-4-oxo-, cyclopropylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

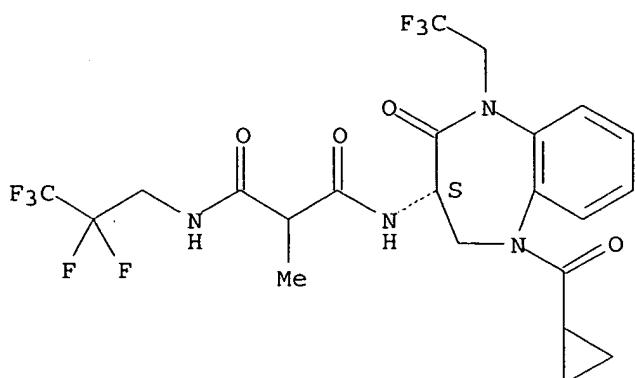
Absolute stereochemistry.



RN 847926-30-1 HCAPLUS

CN Propanediamide, N-[(3S)-5-(cyclopropylcarbonyl)-2,3,4,5-tetrahydro-2-oxo-1-(2,2,2-trifluoroethyl)-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

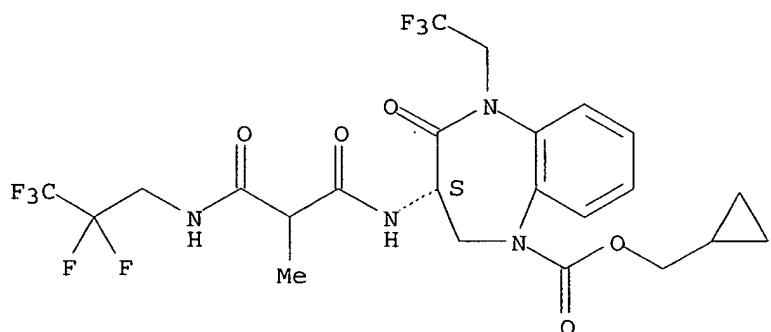
Absolute stereochemistry.



RN 847926-31-2 HCPLUS

CN 1H-1,5-Benzodiazepine-1-carboxylic acid, 2,3,4,5-tetrahydro-3-[(2-methyl-1,3-dioxo-3-[(2,2,3,3-pentafluoropropyl)amino]propyl)amino]-4-oxo-5-(2,2,2-trifluoroethyl)-, cyclopropylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

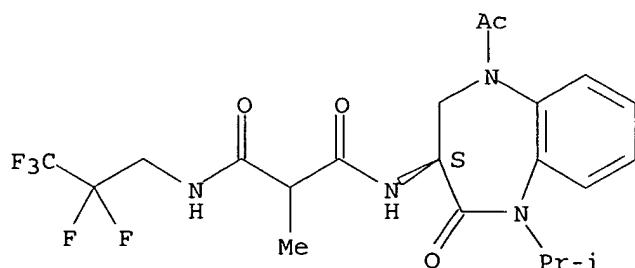
Absolute stereochemistry.



RN 847926-32-3 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-1-(1-methylethyl)-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

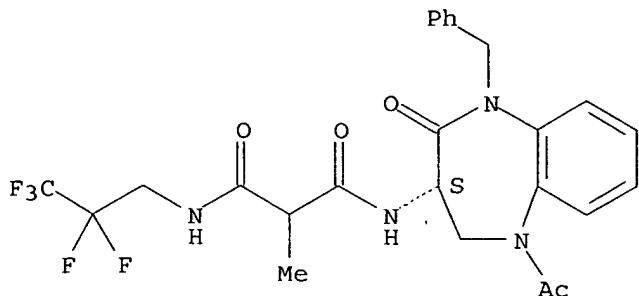


RN 847926-33-4 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-2-oxo-1-(phenylmethyl)-

1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



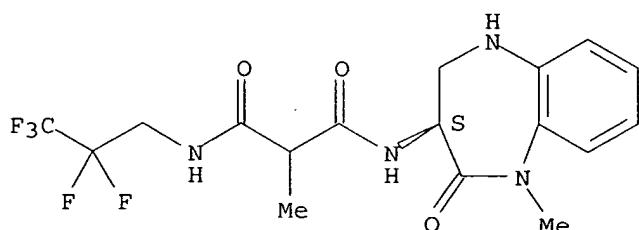
IT 847926-98-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of dibenzoazepinylmalonamides, dibenzooxepinylmalonamides, benzodiazepinylmalonamides, and related compds. as γ -secretase inhibitors for treatment of Alzheimer's disease)

RN 847926-98-1 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 847927-01-9P 847927-02-0P 847927-03-1P
847927-04-2P 847927-05-3P 847927-06-4P
847927-07-5P 847927-08-6P 847927-09-7P
847927-10-0P 847927-11-1P 847927-12-2P
847927-13-3P 847927-14-4P 847927-15-5P
847927-16-6P 847927-17-7P 847927-18-8P
847927-19-9P 847927-20-2P 847927-21-3P
847927-22-4P 847927-23-5P 847927-24-6P
847927-25-7P 847927-26-8P 847927-27-9P
847927-28-0P 847927-29-1P 847927-30-4P
847927-31-5P 847927-32-6P 847927-33-7P
847927-34-8P 847927-35-9P 847927-36-0P
847927-37-1P 847927-47-3P 847927-50-8P
847927-51-9P 847927-52-0P 847927-53-1P
847927-54-2P 847927-55-3P 847927-56-4P
847927-57-5P 847927-58-6P 847927-59-7P
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847927-63-3P 847927-64-4P 847927-65-5P

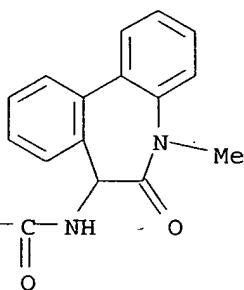
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 847927-72-4P 847927-74-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of dibenzoazepinylmalonamides, dibenzoepoxyethylmalonamides, benzodiazepinylmalonamides, and related compds. as γ -secretase inhibitors for treatment of Alzheimer's disease)

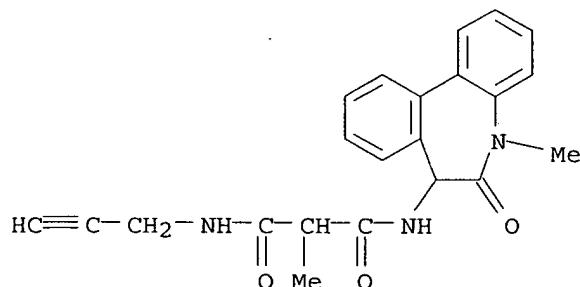
RN 847927-01-9 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-ethyl-2-methyl- (9CI) (CA INDEX NAME)



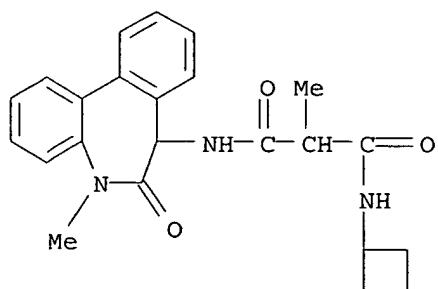
RN 847927-02-0 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-2-propynyl- (9CI) (CA INDEX NAME)



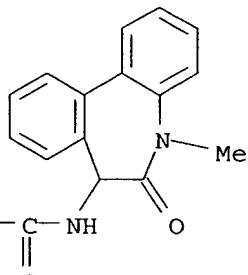
RN 847927-03-1 HCPLUS

CN Propanediamide, N-cyclobutyl-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



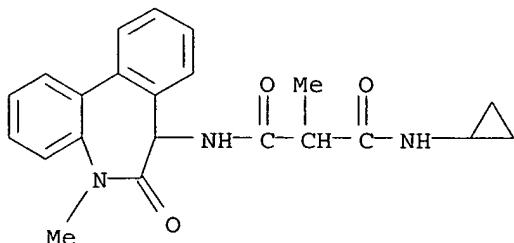
RN 847927-04-2 HCAPLUS

CN Propanediamide, N-(cyanomethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



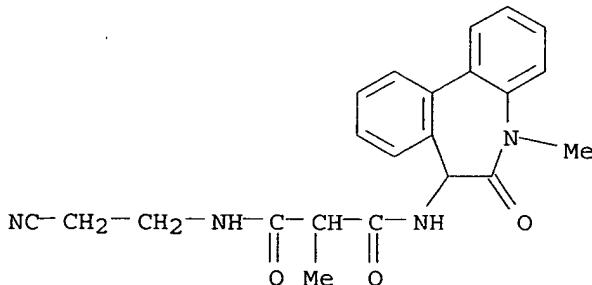
RN 847927-05-3 HCAPLUS

CN Propanediamide, N-cyclopropyl-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



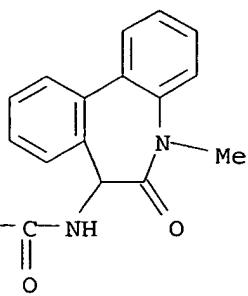
RN 847927-06-4 HCAPLUS

CN Propanediamide, N-(2-cyanoethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



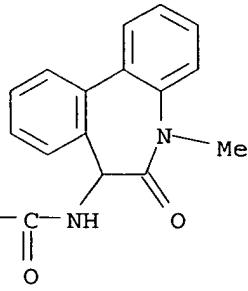
RN 847927-07-5 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-ethoxyethyl)-2-methyl- (9CI) (CA INDEX NAME)



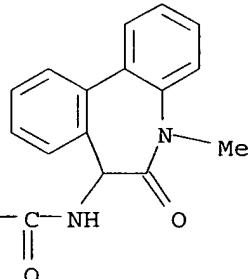
RN 847927-08-6 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



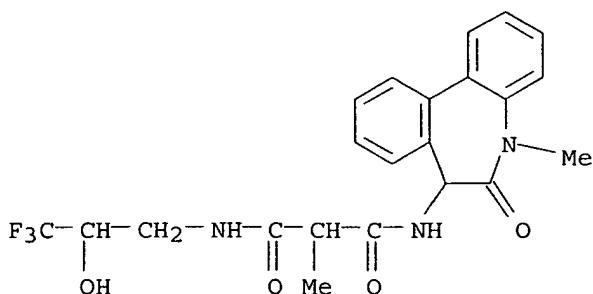
RN 847927-09-7 HCPLUS

CN Glycine, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-3-oxo-β-alanyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



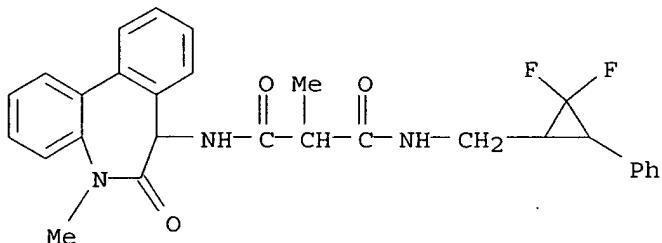
RN 847927-10-0 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(3,3,3-trifluoro-2-hydroxypropyl)-(9CI) (CA INDEX NAME)



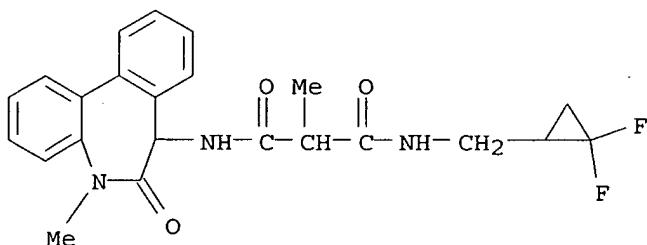
RN 847927-11-1 HCAPLUS

CN Propanediamide, N-[(2,2-difluoro-3-phenylcyclopropyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



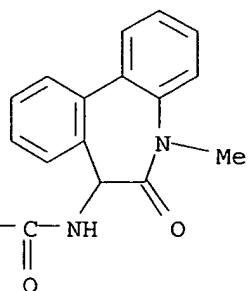
RN 847927-12-2 HCAPLUS

CN Propanediamide, N-[(2,2-difluorocyclopropyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



RN 847927-13-3 HCAPLUS

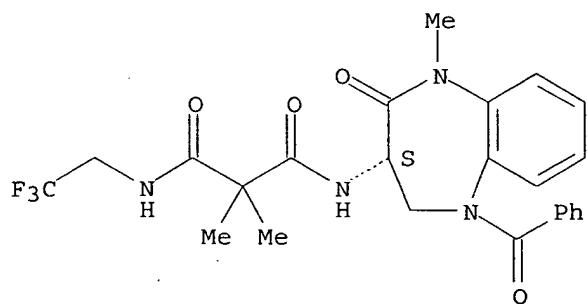
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz [b,d]azepin-7-yl)-2-phenyl-N'-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)



RN 847927-14-4 HCAPLUS

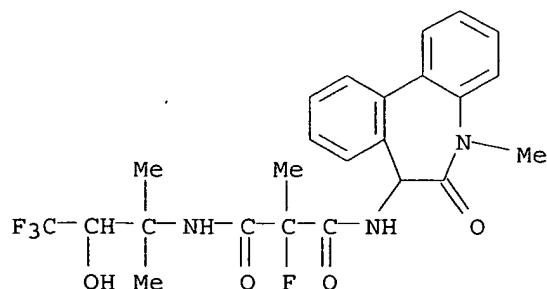
CN Propanediamide, N-[(3S)-5-benzoyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2,2-dimethyl-N'-(2,2,2-trifluoroethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



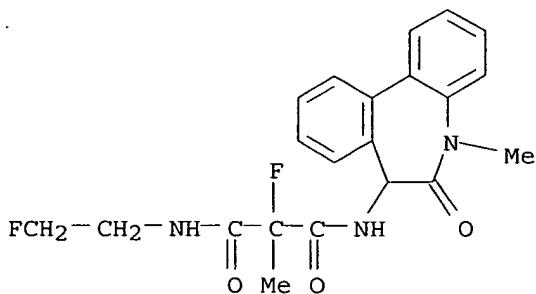
RN 847927-15-5 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz [b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(3,3,3-trifluoro-2-hydroxy-1,1-dimethylpropyl)-(9CI)
(CA INDEX NAME)



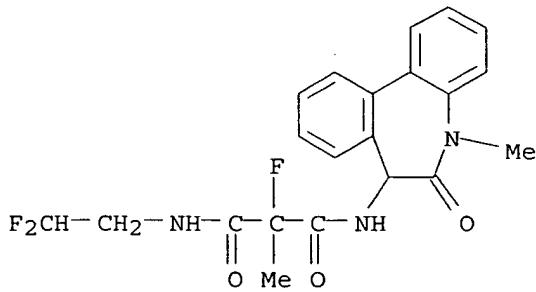
RN 847927-16-6 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz [b,d]azepin-7-yl)-2-fluoro-N'-(2-fluoroethyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 847927-17-7 HCAPLUS

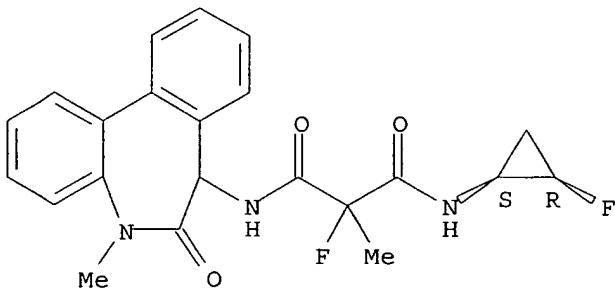
CN Propanediamide, N-(2,2-difluoroethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl- (9CI) (CA INDEX NAME)



RN 847927-18-8 HCAPLUS

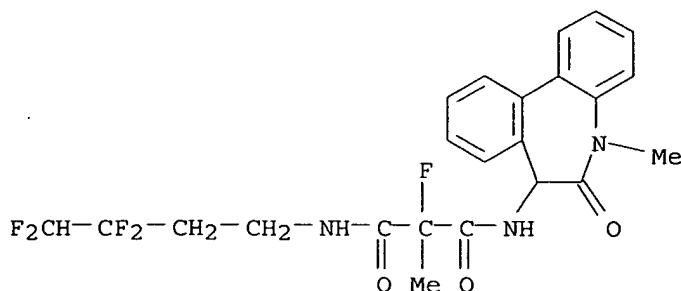
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-N'-(1R,2S)-2-fluorocyclopropyl-2-methyl-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



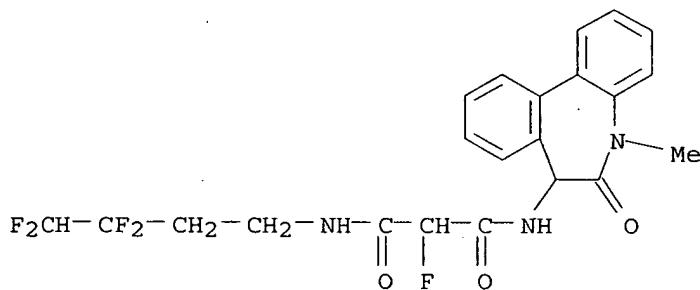
RN 847927-19-9 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl-N'-(3,3,4,4-tetrafluorobutyl)- (9CI) (CA INDEX NAME)



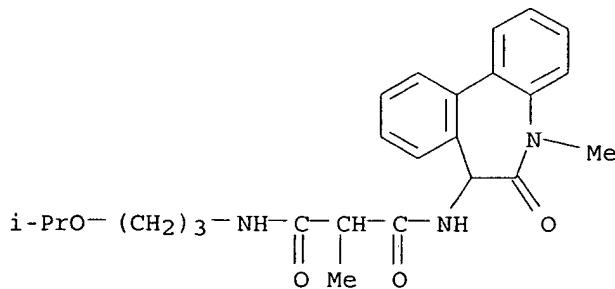
RN 847927-20-2 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-N'-(3,3,4,4-tetrafluorobutyl)- (9CI) (CA INDEX NAME)



RN 847927-21-3 HCPLUS

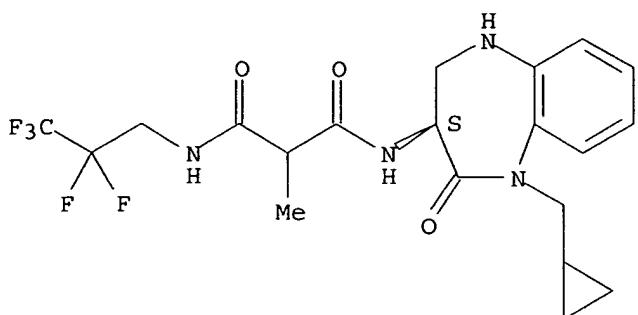
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(3-(1-methylethoxy)propyl)- (9CI) (CA INDEX NAME)



RN 847927-22-4 HCPLUS

CN Propanediamide, N-[(3S)-1-(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

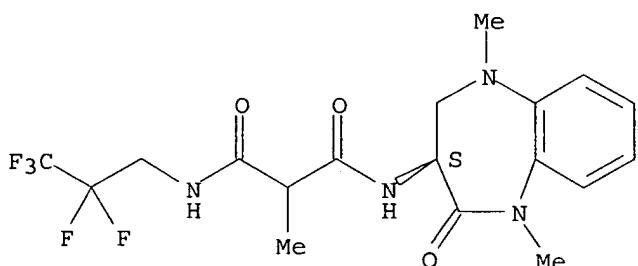
Absolute stereochemistry.



RN 847927-23-5 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-1,5-dimethyl-2-oxo-1H-1,5-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)

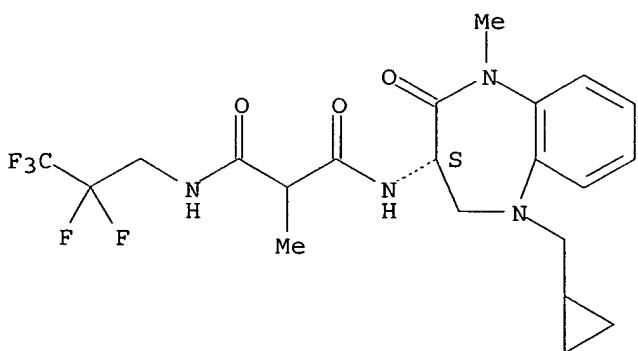
Absolute stereochemistry.



RN 847927-24-6 HCPLUS

CN Propanediamide, N-[(3S)-5-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

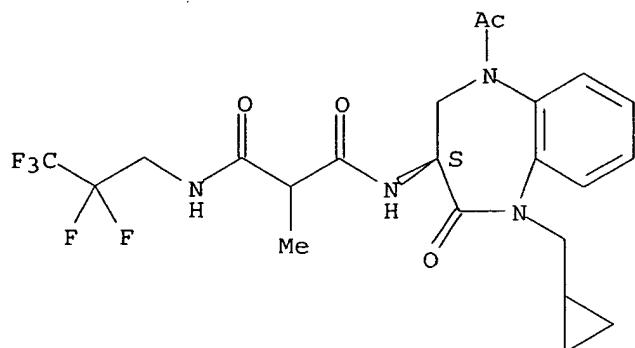
Absolute stereochemistry.



RN 847927-25-7 HCPLUS

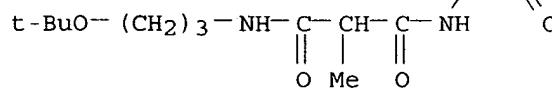
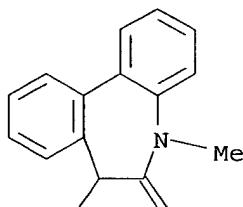
CN Propanediamide, N-[(3S)-5-acetyl-1-(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847927-26-8 HCAPLUS

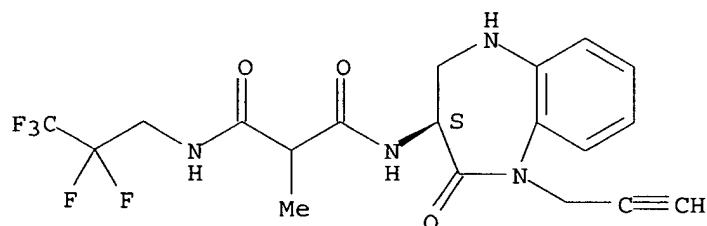
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(3-(1,1-dimethylethoxy)propyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 847927-27-9 HCAPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-2-oxo-1-(2-propynyl)-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)

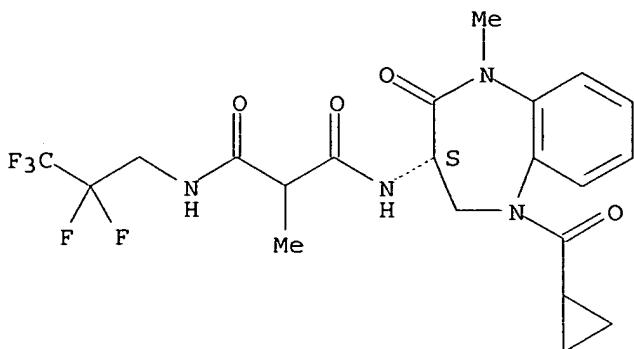
Absolute stereochemistry.



RN 847927-28-0 HCAPLUS

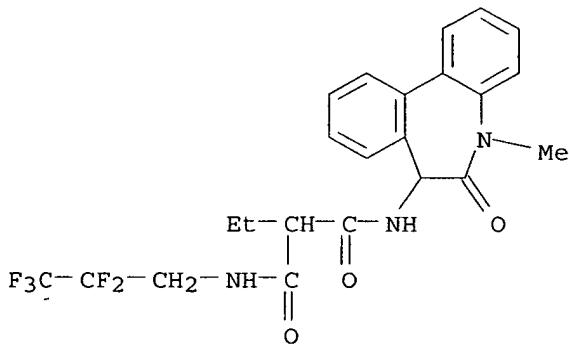
CN Propanediamide, N-[(3S)-5-(cyclopropylcarbonyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



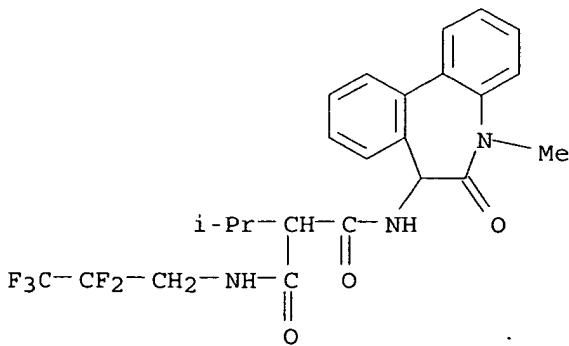
RN 847927-29-1 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-ethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847927-30-4 HCAPLUS

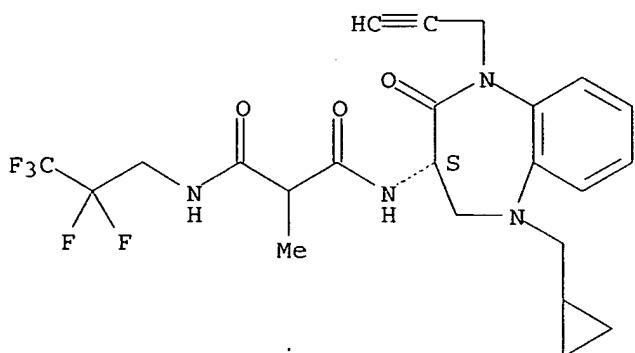
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-(1-methylethyl)-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)



RN 847927-31-5 HCAPLUS

CN Propanediamide, N-[{(3S)-5-(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1-(2-propynyl)-1H-1,5-benzodiazepin-3-yl}-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)]-(9CI) (CA INDEX NAME)

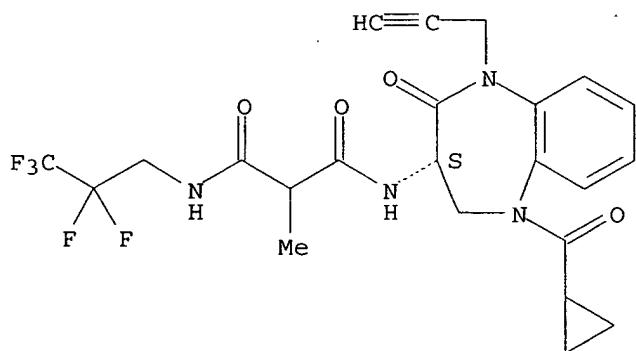
Absolute stereochemistry.



RN 847927-32-6 HCAPLUS

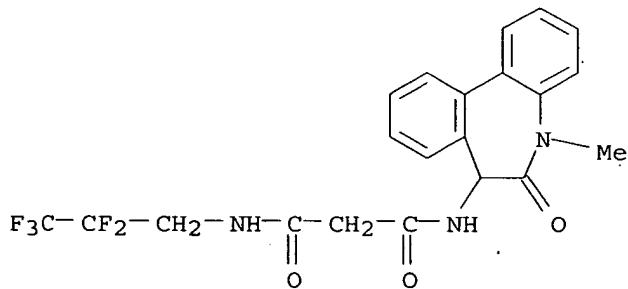
CN Propanediamide, N-[{(3S)-5-(cyclopropylcarbonyl)-2,3,4,5-tetrahydro-2-oxo-1-(2-propynyl)-1H-1,5-benzodiazepin-3-yl}-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



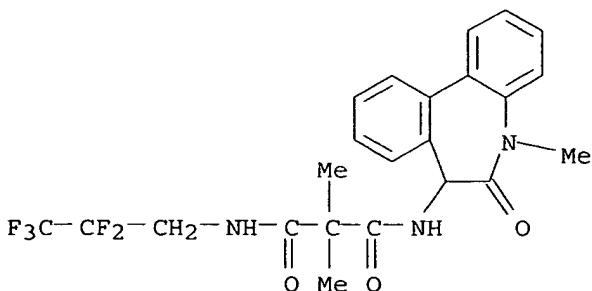
RN 847927-33-7 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

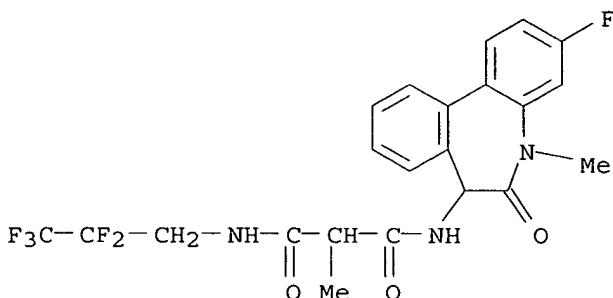


RN 847927-34-8 HCAPLUS

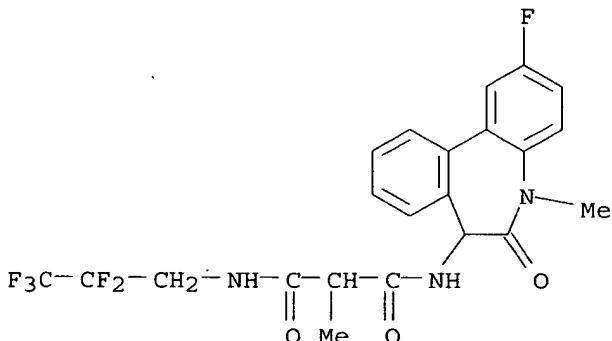
CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



RN 847927-35-9 HCPLUS

CN Propanediamide, N-(3-fluoro-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI)
(CA INDEX NAME)

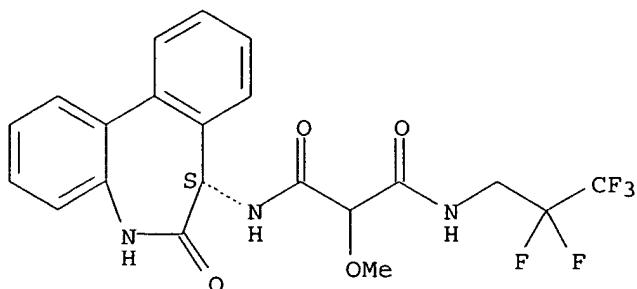
RN 847927-36-0 HCPLUS

CN Propanediamide, N-(2-fluoro-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI)
(CA INDEX NAME)

RN 847927-37-1 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methoxy-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI)
(CA INDEX NAME)

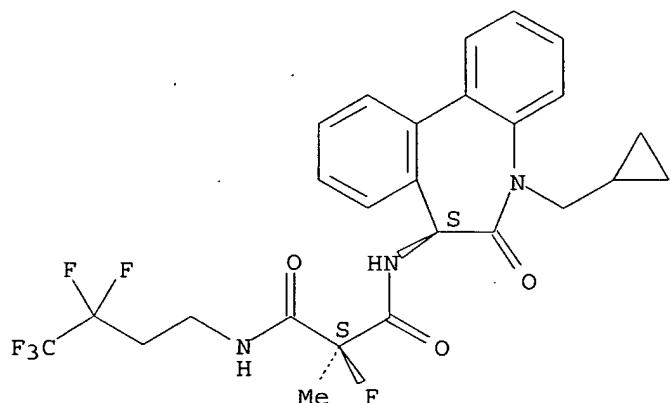
Absolute stereochemistry.



RN 847927-47-3 HCPLUS

CN Propanediamide, N-[(7S)-5-(cyclopropylmethyl)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-(2S)-(9CI) (CA INDEX NAME)

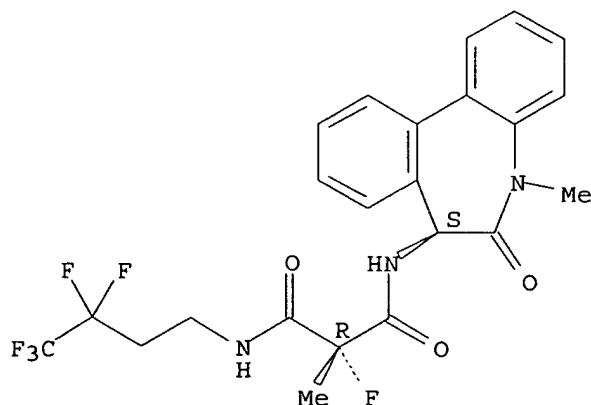
Absolute stereochemistry.



RN 847927-50-8 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-(2R)-(9CI) (CA INDEX NAME)

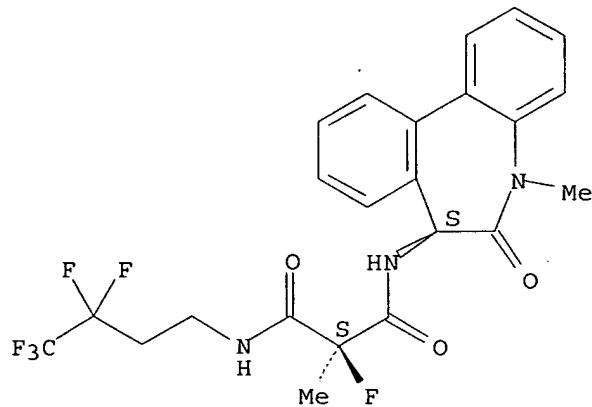
Absolute stereochemistry.



RN 847927-51-9 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-, (2S)- (9CI) (CA INDEX NAME)

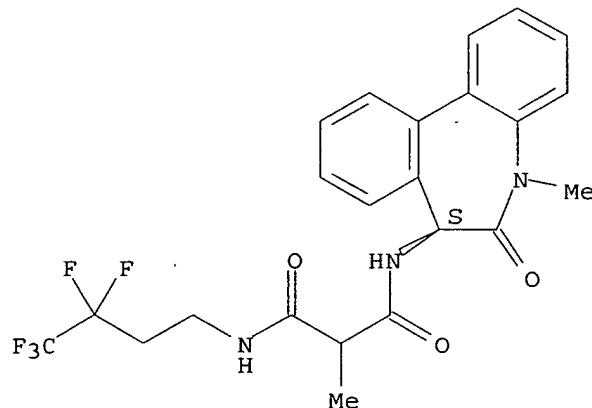
Absolute stereochemistry.



RN 847927-52-0 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)- (9CI) (CA INDEX NAME)

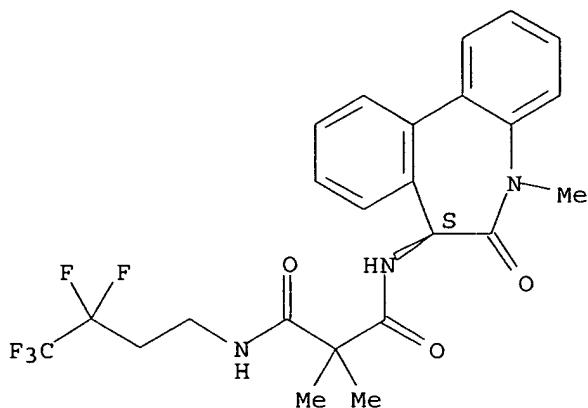
Absolute stereochemistry.



RN 847927-53-1 HCAPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(3,3,4,4,4-pentafluorobutyl)- (9CI) (CA INDEX NAME)

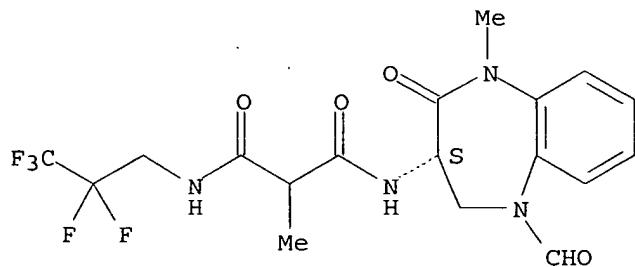
Absolute stereochemistry.



RN 847927-54-2 HCPLUS

CN Propanediamide, N-[(3S)-5-formyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

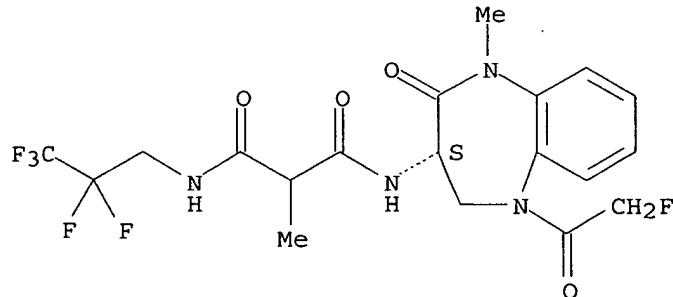
Absolute stereochemistry.



RN 847927-55-3 HCPLUS

CN Propanediamide, N-[(3S)-5-(fluoroacetyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

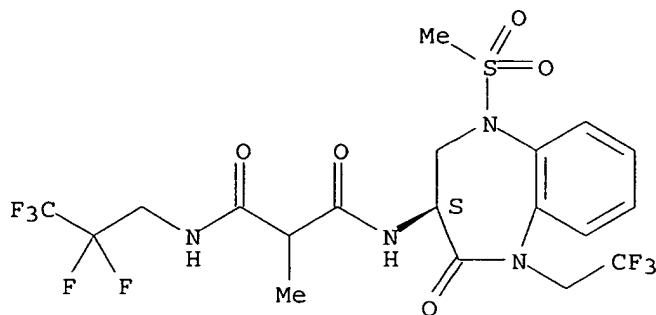


RN 847927-56-4 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-5-(methylsulfonyl)-2-oxo-1-(2,2,2-trifluoroethyl)-1H-1,5-

benzodiazepin-3-yl] - (9CI) (CA INDEX NAME)

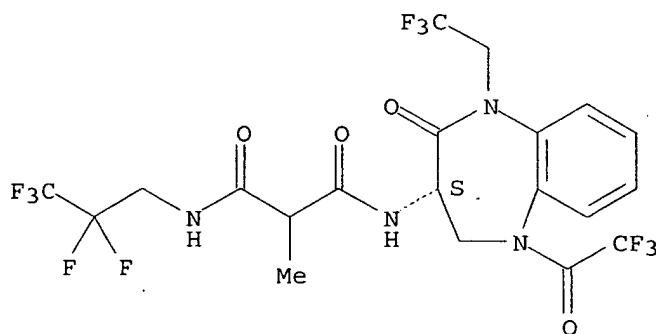
Absolute stereochemistry.



RN 847927-57-5 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-(3S)-2,3,4,5-tetrahydro-2-oxo-5-(trifluoroacetyl)-1-(2,2,2-trifluoroethyl)-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)

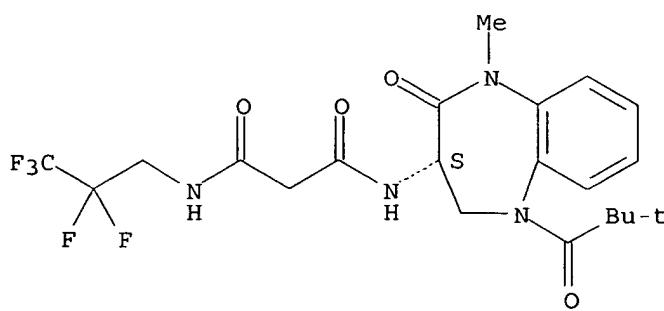
Absolute stereochemistry.



RN 847927-58-6 HCPLUS

CN Propanediamide, N-[(3S)-5-(2,2-dimethyl-1-oxopropyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

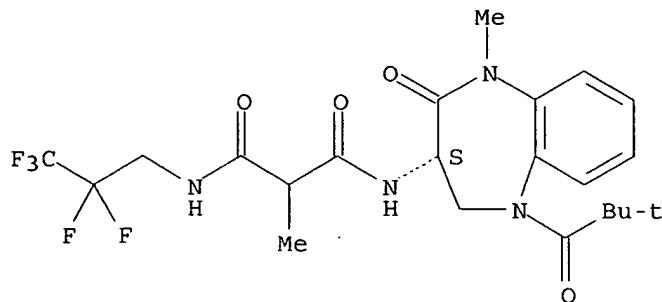


RN 847927-59-7 HCPLUS

CN Propanediamide, N-[(3S)-5-(2,2-dimethyl-1-oxopropyl)-2,3,4,5-tetrahydro-1-

methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

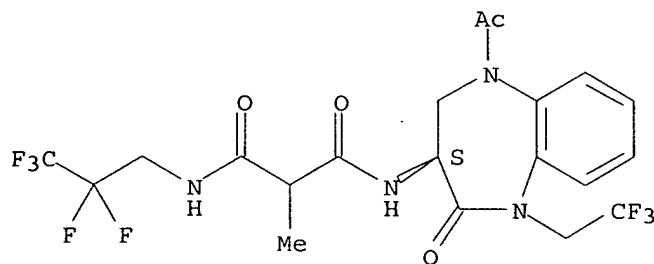
Absolute stereochemistry.



RN 847927-60-0 HCAPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-2-oxo-1-(2,2,2-trifluoromethyl)-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

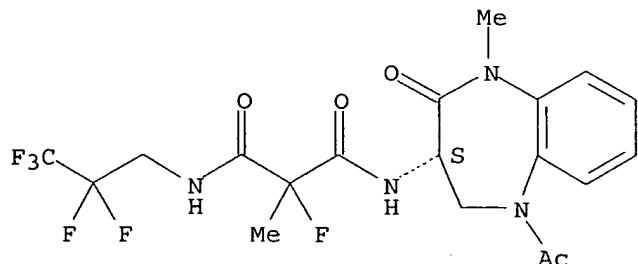
Absolute stereochemistry.



RN 847927-61-1 HCAPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-fluoro-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

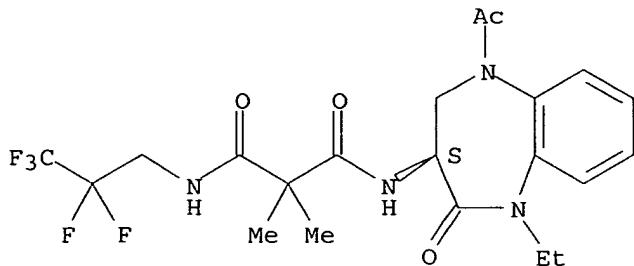
Absolute stereochemistry.



RN 847927-62-2 HCAPLUS

CN Propanediamide, N-[(3S)-5-acetyl-1-ethyl-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

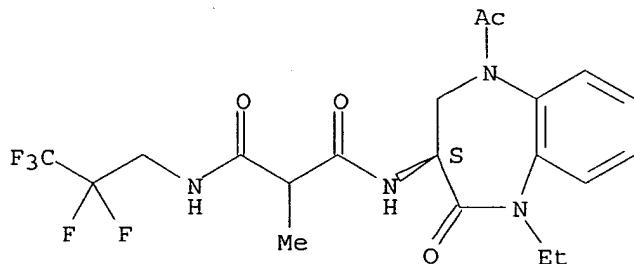
Absolute stereochemistry.



RN 847927-63-3 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-1-ethyl-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

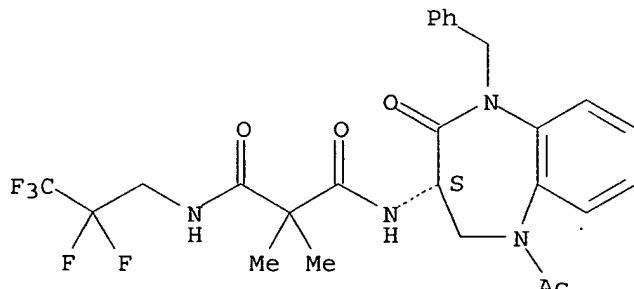
Absolute stereochemistry.



RN 847927-64-4 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-2-oxo-1-(phenylmethyl)-1H-1,5-benzodiazepin-3-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

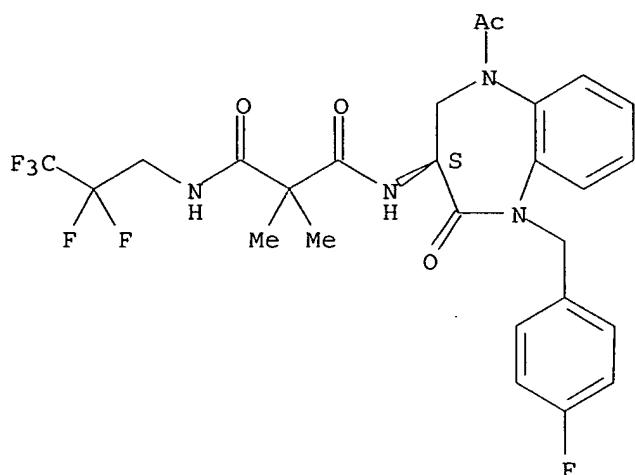
Absolute stereochemistry.



RN 847927-65-5 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-1-[(4-fluorophenyl)methyl]-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2,2-dimethyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

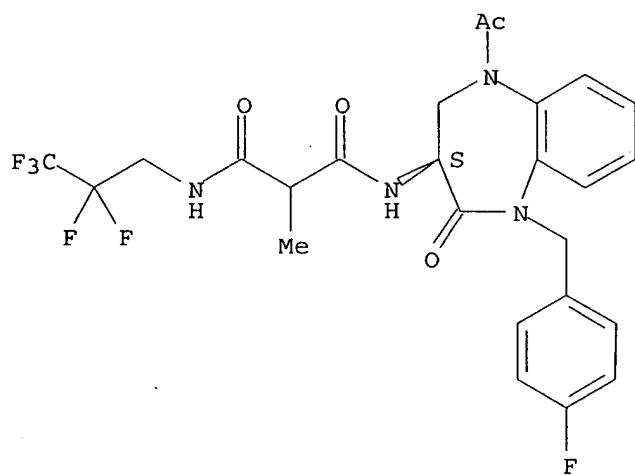
Absolute stereochemistry.



RN 847927-66-6 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-1-[(4-fluorophenyl)methyl]-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(9CI) (CA INDEX NAME)

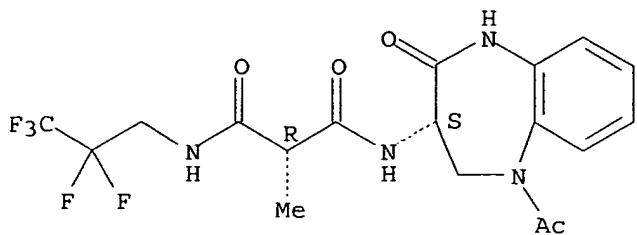
Absolute stereochemistry.



RN 847927-67-7 HCPLUS

CN Propanediamide, N-[(3S)-1-acetyl-2,3,4,5-tetrahydro-4-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-(2R)-(9CI) (CA INDEX NAME)

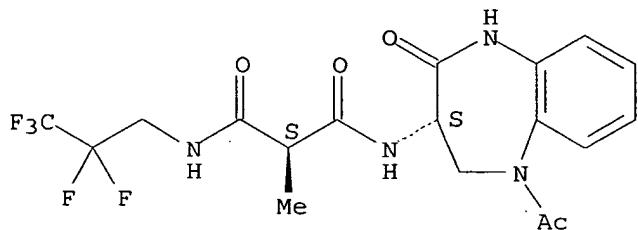
Absolute stereochemistry.



RN 847927-68-8 HCPLUS

CN Propanediamide, N-[(3S)-1-acetyl-2,3,4,5-tetrahydro-4-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2S)-(9CI) (CA INDEX NAME)

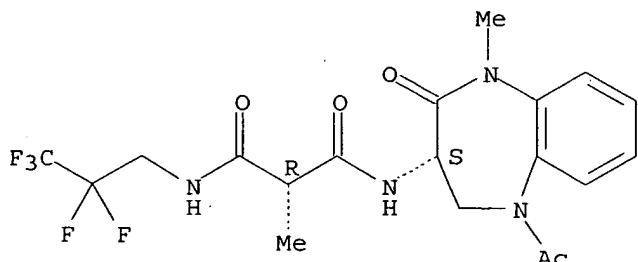
Absolute stereochemistry.



RN 847927-69-9 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2R)-(9CI) (CA INDEX NAME)

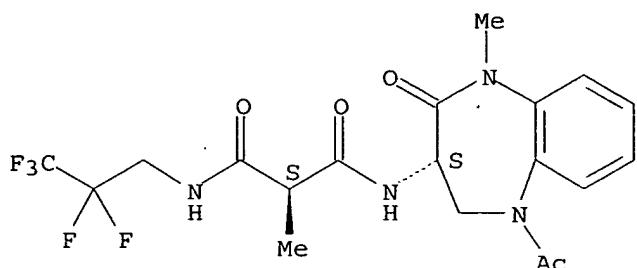
Absolute stereochemistry.



RN 847927-70-2 HCPLUS

CN Propanediamide, N-[(3S)-5-acetyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-2-methyl-N'-(2,2,3,3,3-pentafluoropropyl)-, (2S)-(9CI) (CA INDEX NAME)

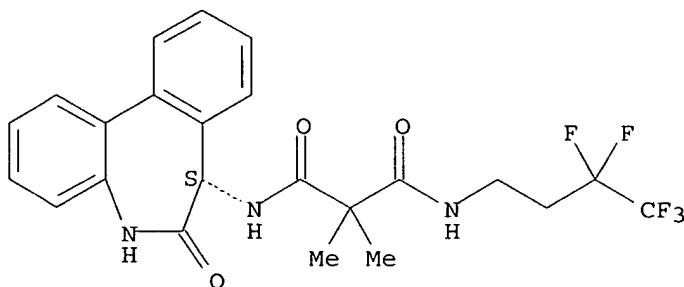
Absolute stereochemistry.



RN 847927-71-3 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2,2-dimethyl-N'-(3,3,4,4,4-pentafluorobutyl)-(9CI) (CA INDEX NAME)

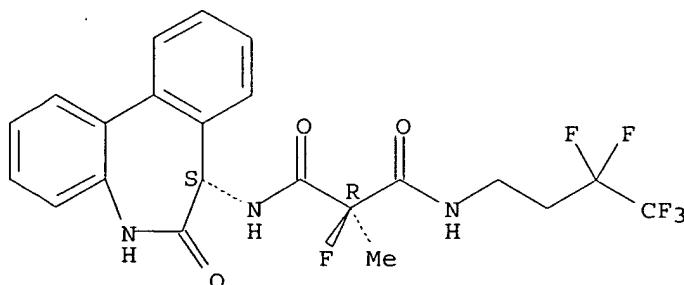
Absolute stereochemistry.



RN 847927-72-4 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(3,3,4,4,4-pentafluorobutyl)-(2R)-(9CI) (CA INDEX NAME)

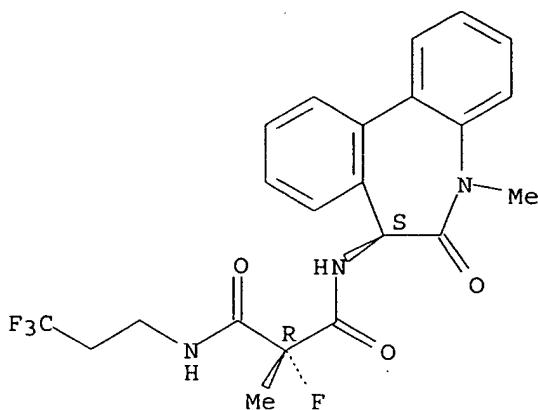
Absolute stereochemistry.



RN 847927-74-6 HCPLUS

CN Propanediamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-fluoro-2-methyl-N'-(3,3,3-trifluoropropyl)-(2R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



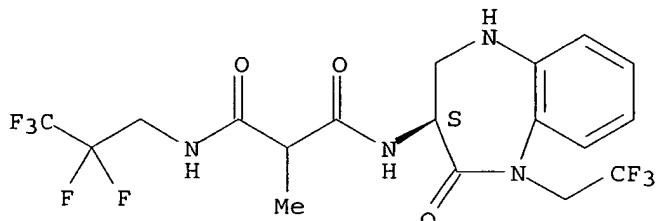
IT 847926-61-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of dibenzoazepinylmalonamides, dibenzooxepinylmalonamides, benzodiazepinylmalonamides, and related compds. as γ -secretase inhibitors for treatment of Alzheimer's disease)

RN 847926-61-8 HCPLUS

CN Propanediamide, 2-methyl-N-(2,2,3,3,3-pentafluoropropyl)-N'-([(3S)-2,3,4,5-tetrahydro-2-oxo-1-(2,2,2-trifluoroethyl)-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L98 ANSWER 2 OF 25 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:675740 HCPLUS

DOCUMENT NUMBER: 141:206827

TITLE: Preparation of malonamides and related compounds as γ -secretase inhibitors for the treatment of Alzheimer's disease.

INVENTOR(S): Galley, Guido; Goergler, Annick; Jacobsen, Helmut; Kitas, Eric Argirios; Peters, Jens-Uwe

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004069826	A1	20040819	WO 2004-EP674	20040127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
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AU 2004210036	A1	20040819	AU 2004-210036	20040127
CA 2514267	AA	20040819	CA 2004-2514267	20040127
EP 1592684	A1	20051109	EP 2004-705404	20040127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007262	A	20060131	BR 2004-7262	20040127
CN 1745076	A	20060308	CN 2004-80003305	20040127
JP 2006516556	T2	20060706	JP 2006-500017	20040127
US 2004220222	A1	20041104	US 2004-767784	20040129
NO 2005003627	A	20050810	NO 2005-3627	20050726
PRIORITY APPLN. INFO.:			EP 2003-2190	A 20030204
			WO 2004-EP674	W 20040127

OTHER SOURCE(S): MARPAT 141:206827

ED Entered STN: 19 Aug 2004

AB Title compds. I [L = bond, (CH₂)₁₋₂, CH(CH₃), etc.; C = cyclic ring, e.g., Ph, pyridinyl, furanyl, etc.; X = (R₂)_{1,2,3}; (R₂)_{1,2,3} = H, OH, halo, etc.; R₁, R_{1'} = H, alkyl, halo, etc.; R₁₄ = H, alkyl, (CH₂)₂₀H, etc.; A = substituted 5,7-dihydro-6H-dibenz[b,d]azepin-6-ones, 1,3-dihydro-5-phenyl-1,4-benzodiazepin-2-ones, 3,4-dihydro-2-quinolinones, etc.] and their pharmaceutically acceptable salts and formulations were prepared. For example, coupling of 3-amino-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one and malonamic acid II, e.g., prepared from di-Et Me malonate in 3-steps, afforded malonamide III in 67% yield. In γ -secretase inhibition assays, 37-examples of compds. I exhibited IC₅₀ values ranging from 0.003-0.11 μ M, the IC₅₀ value of malonamide III was 0.83 μ M. Compds. I are claimed useful for the treatment of Alzheimer's disease.

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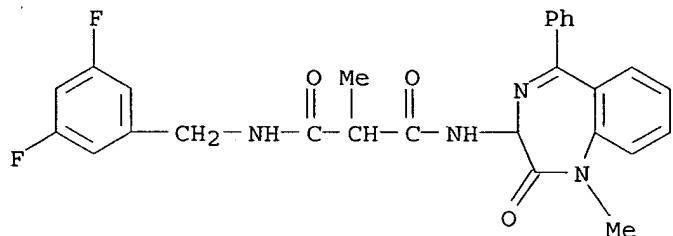
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of malonamides and related compds. as γ -secretase inhibitors for the treatment of Alzheimer's disease.)

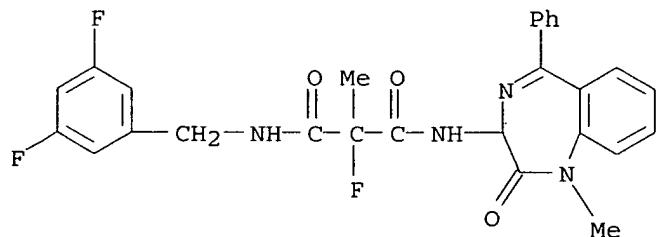
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CN Propanediamide, N-[{(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl- (9CI) (CA INDEX NAME)



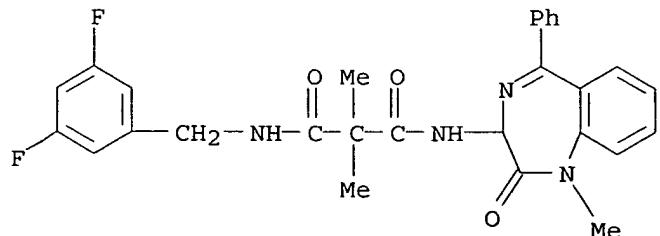
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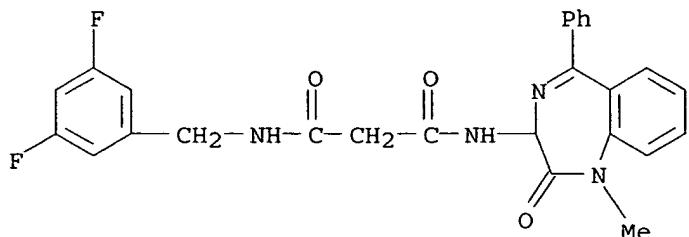
RN 741672-57-1 HCPLUS

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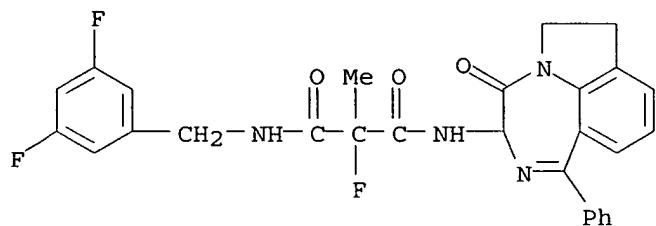
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



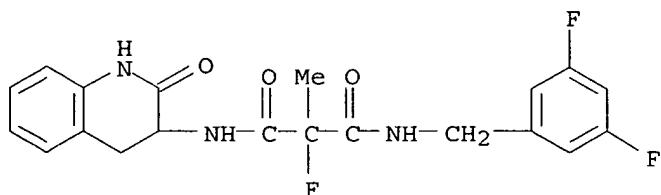
RN 741672-59-3 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-fluoro-2-methyl-N'-(3,4,6,7-tetrahydro-4-oxo-1-phenylpyrrolo[3,2,1-jk][1,4]benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



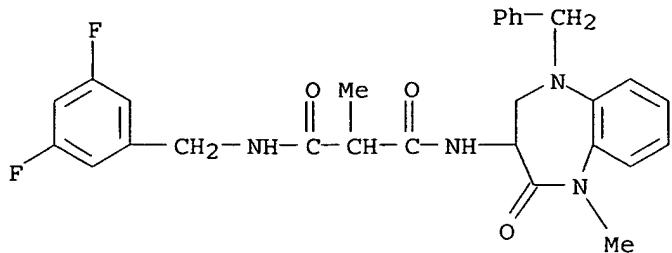
RN 741672-65-1 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-fluoro-2-methyl-N'-(1,2,3,4-tetrahydro-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)



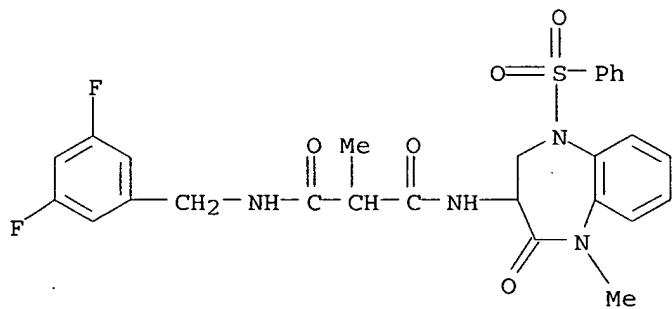
RN 741672-66-2 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-[2,3,4,5-tetrahydro-1-methyl-2-oxo-5-(phenylmethyl)-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)



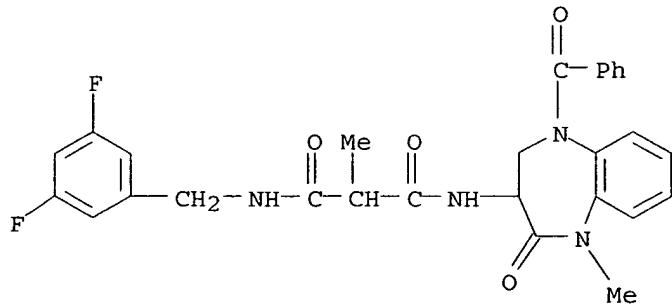
RN 741672-68-4 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-(2,3,4,5-tetrahydro-1-methyl-2-oxo-5-(phenylsulfonyl)-1H-1,5-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



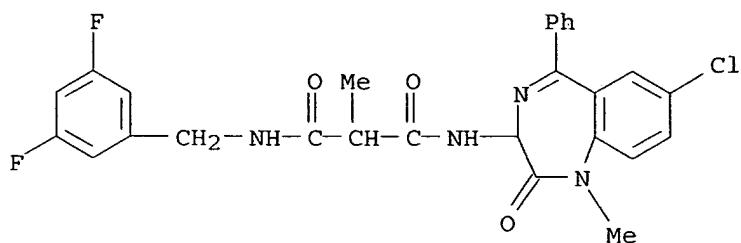
RN 741672-69-5 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-(5-benzoyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



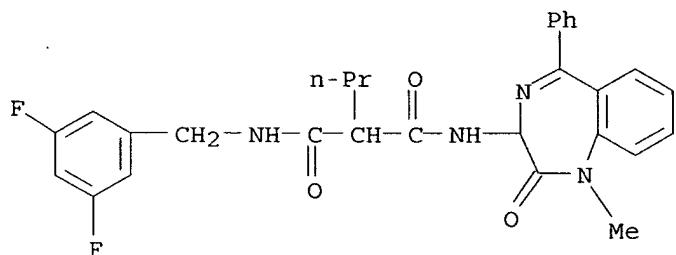
RN 741672-70-8 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-(7-chloro-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



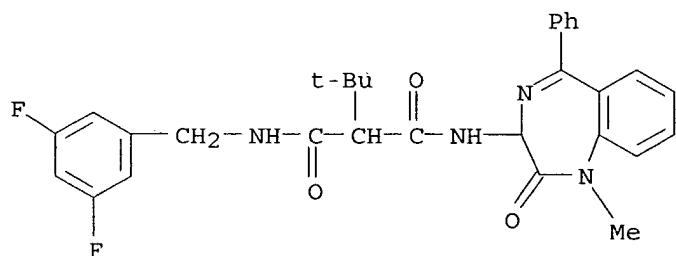
RN 741673-60-9 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-propyl- (9CI) (CA INDEX NAME)



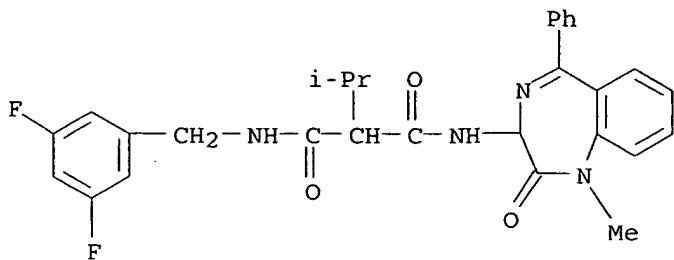
RN 741673-61-0 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



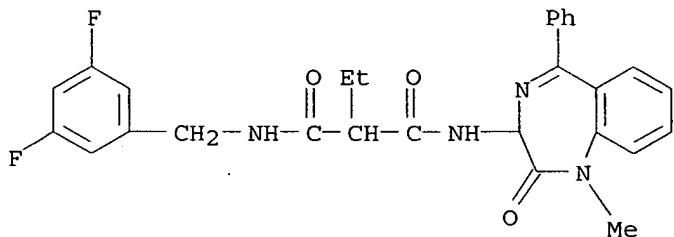
RN 741673-62-1 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



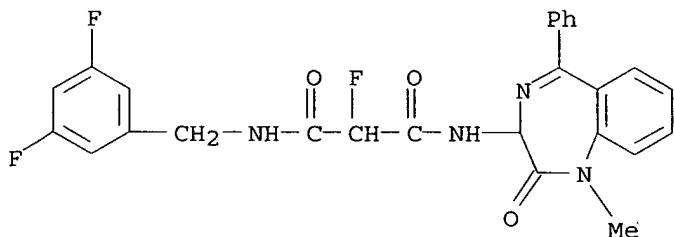
RN 741673-63-2 HCPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-ethyl- (9CI) (CA INDEX NAME)



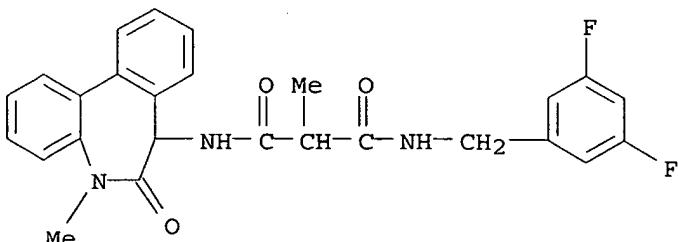
RN 741673-64-3 HCPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-fluoro- (9CI) (CA INDEX NAME)



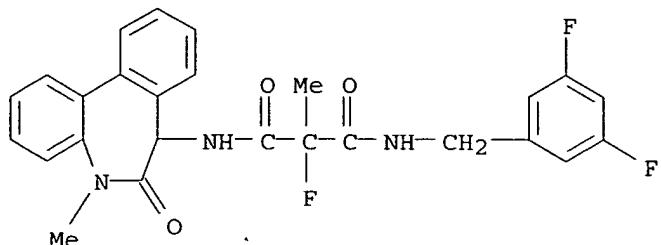
RN 741673-65-4 HCPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



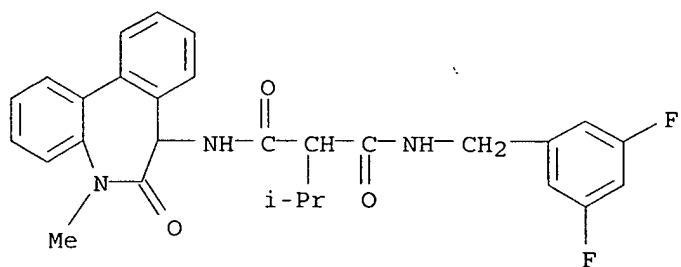
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro-2-methyl- (9CI) (CA INDEX NAME)



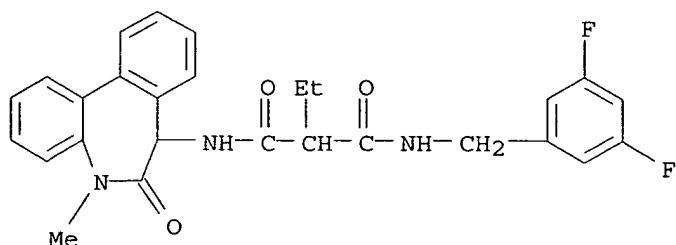
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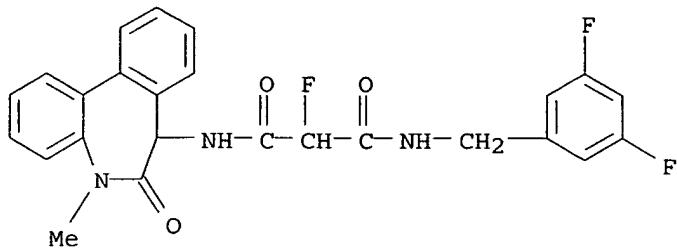
RN 741673-68-7 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-ethyl- (9CI) (CA INDEX NAME)



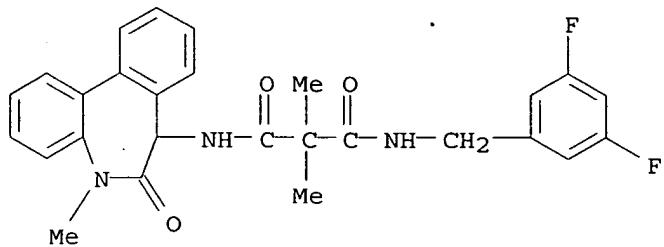
RN 741673-69-8 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-fluoro- (9CI) (CA INDEX NAME)



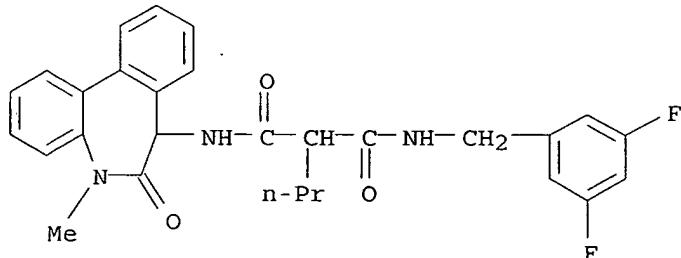
RN 741673-70-1 HCPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2,2-dimethyl- (9CI) (CA INDEX NAME)



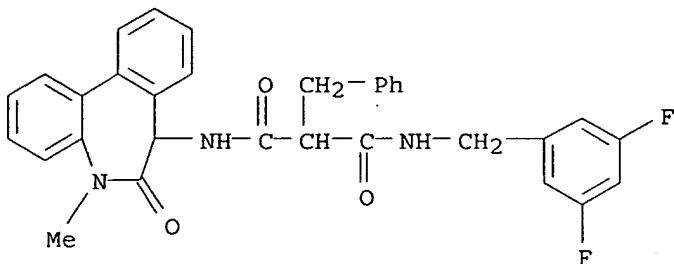
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-propyl- (9CI) (CA INDEX NAME)



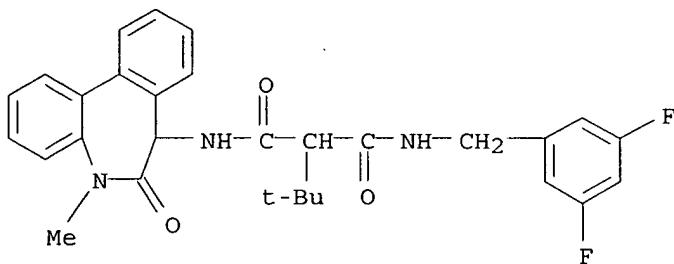
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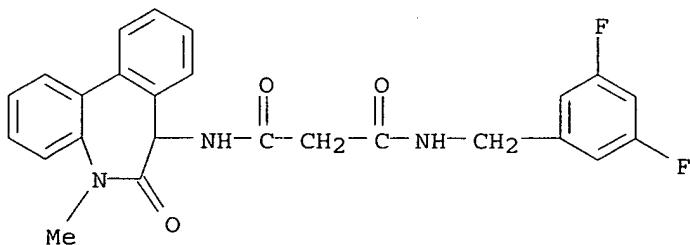
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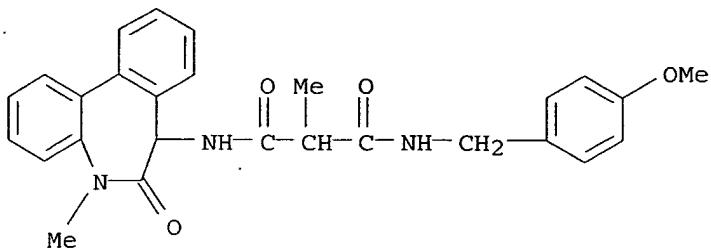
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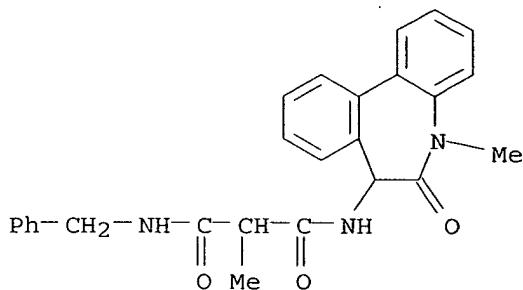
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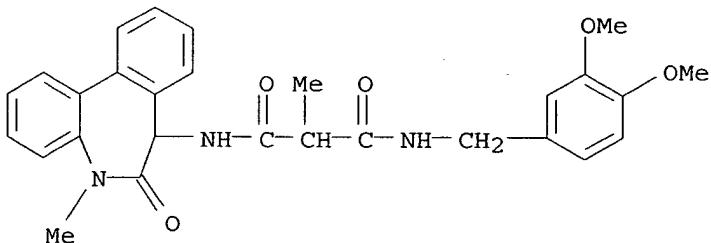
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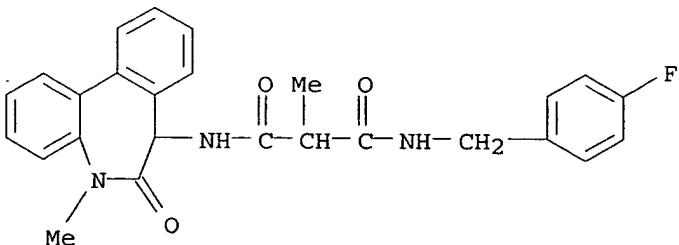
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CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(3,4-dimethoxyphenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



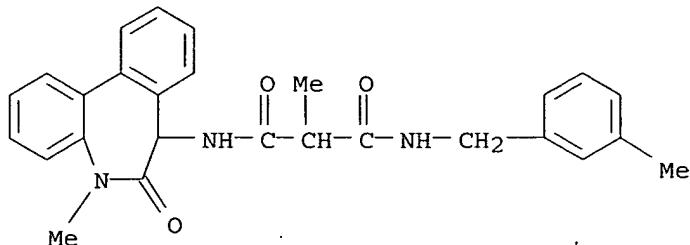
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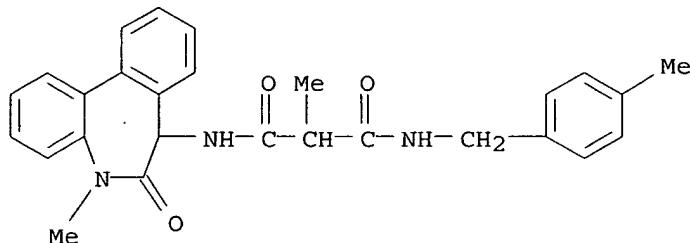
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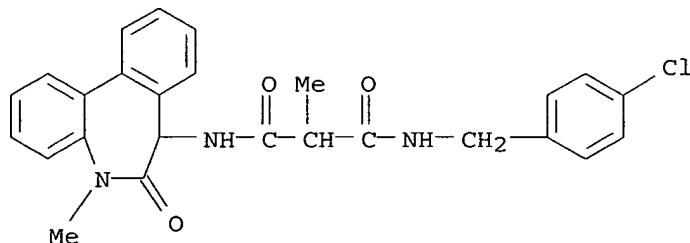
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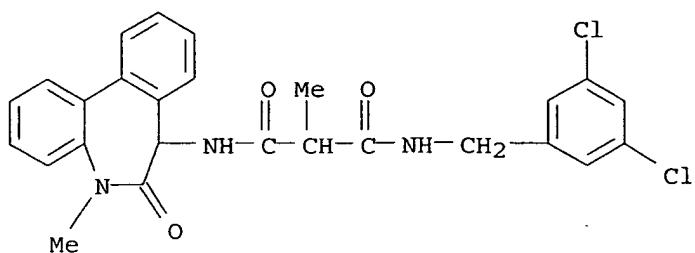
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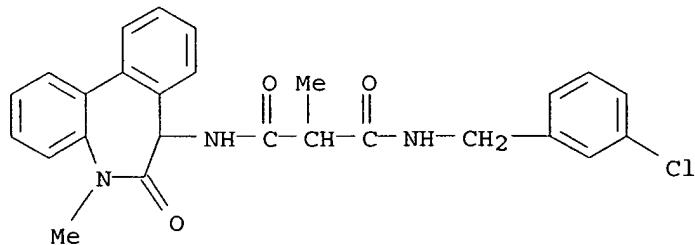


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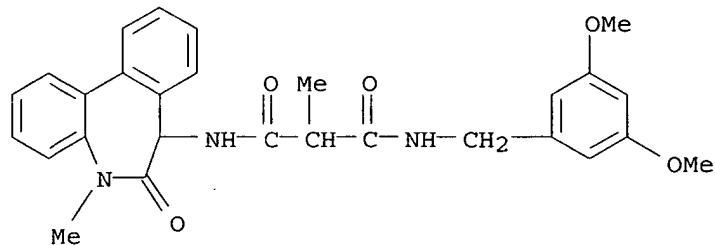
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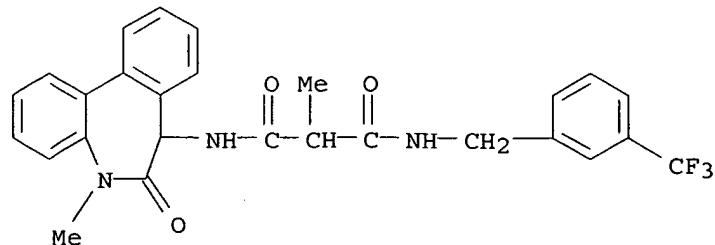
RN 741673-83-6 HCPLUS
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RN 741673-84-7 HCPLUS
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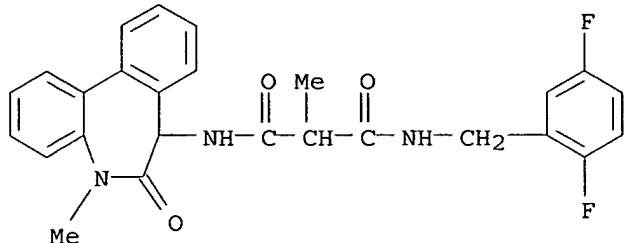


RN 741673-85-8 HCPLUS
 CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



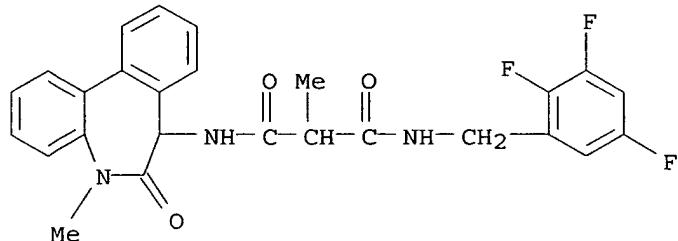
RN 741673-86-9 HCAPLUS

CN Propanediamide, N-[(2,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



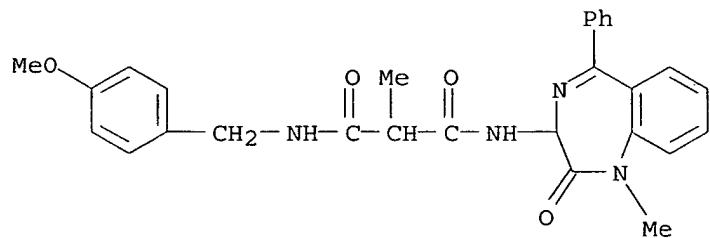
RN 741673-87-0 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2,3,5-trifluorophenyl)methyl- (9CI) (CA INDEX NAME)



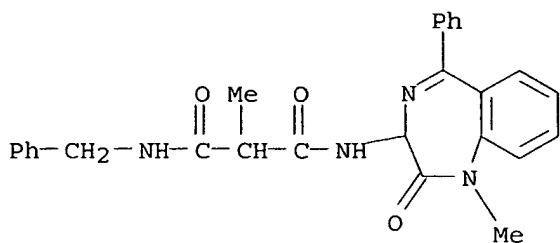
RN 741673-88-1 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-methoxyphenyl)methyl-2-methyl- (9CI) (CA INDEX NAME)



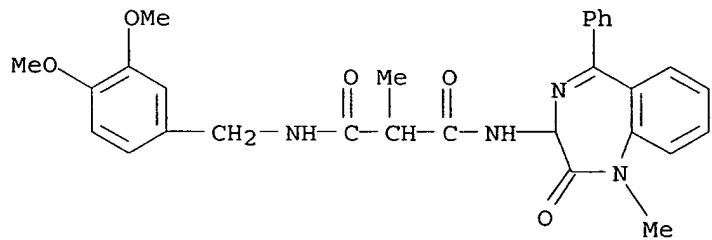
RN 741673-89-2 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



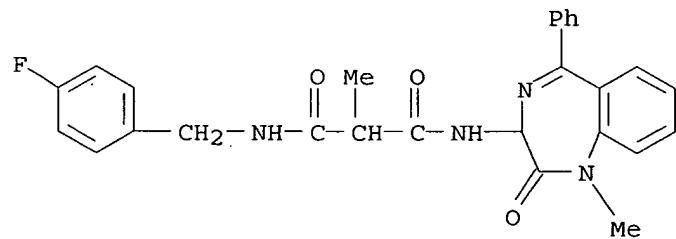
RN 741673-90-5 HCPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3,4-dimethoxyphenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



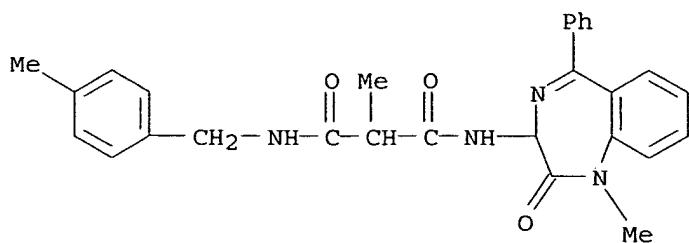
RN 741673-91-6 HCPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-fluorophenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



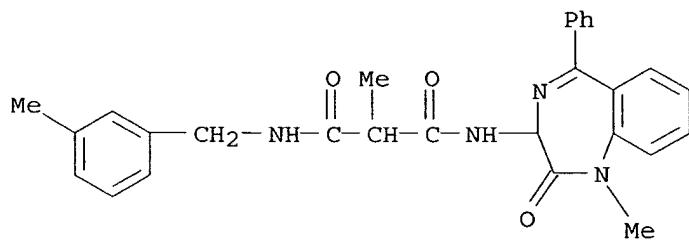
RN 741673-92-7 HCPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl-N'-(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



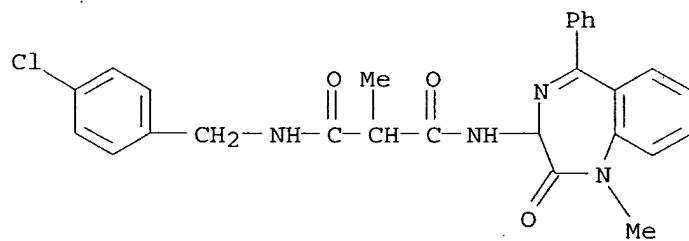
RN 741673-93-8 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl-N'-(3-methylphenyl)methyl- (9CI) (CA INDEX NAME)



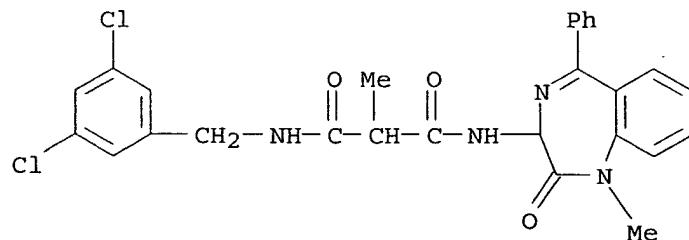
RN 741673-94-9 HCAPLUS

CN Propanediamide, N-[{(4-chlorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl- (9CI) (CA INDEX NAME)



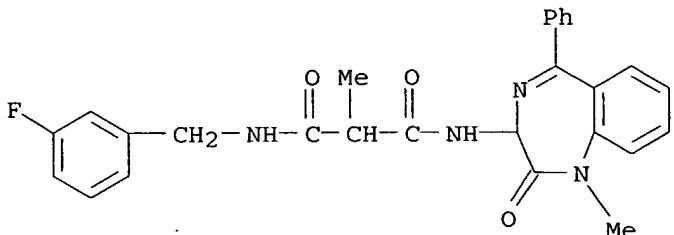
RN 741673-95-0 HCAPLUS

CN Propanediamide, N-[{(3,5-dichlorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl- (9CI) (CA INDEX NAME)



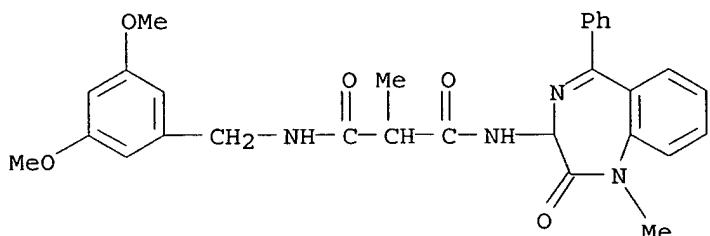
RN 741673-96-1 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-fluorophenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



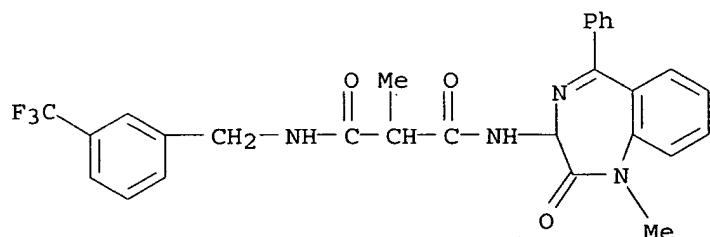
RN 741673-97-2 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3,5-dimethoxyphenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



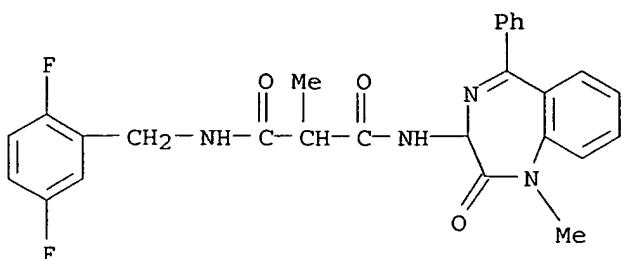
RN 741673-98-3 HCAPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl-N'-(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

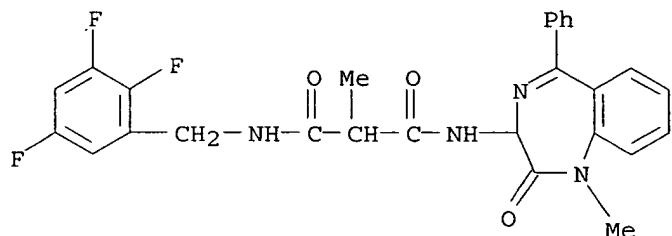


RN 741673-99-4 HCAPLUS

CN Propanediamide, N-[(2,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl- (9CI) (CA INDEX NAME)

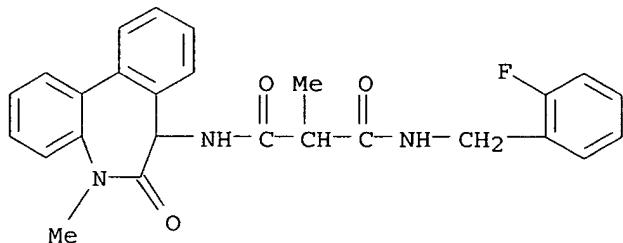


RN 741674-00-0 HCPLUS

CN Propanediamide, N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-2-methyl-N'-(2,3,5-trifluorophenyl)methyl]- (9CI)
(CA INDEX NAME)

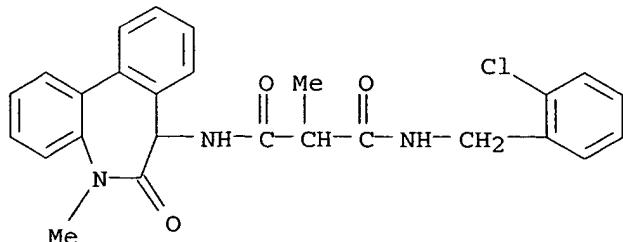
RN 741674-04-4 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-fluorophenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)



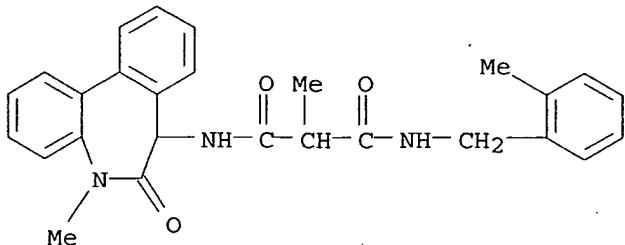
RN 741674-05-5 HCPLUS

CN Propanediamide, N-[(2-chlorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



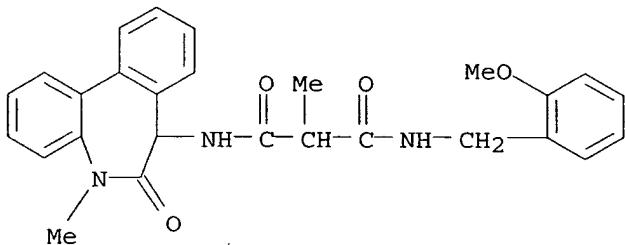
RN 741674-06-6 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2-methylphenyl)methyl- (9CI) (CA INDEX NAME)



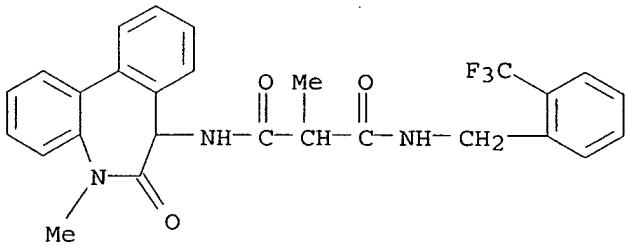
RN 741674-07-7 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-methoxyphenyl)methyl-2-methyl- (9CI) (CA INDEX NAME)



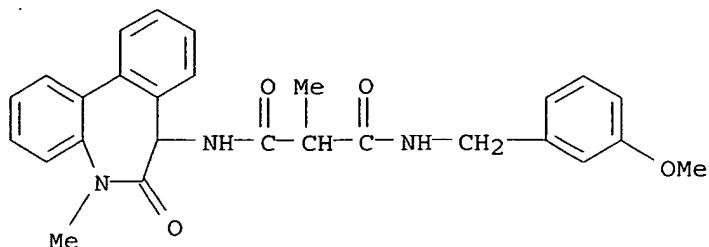
RN 741674-08-8 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2-(trifluoromethyl)phenyl)methyl- (9CI) (CA INDEX NAME)



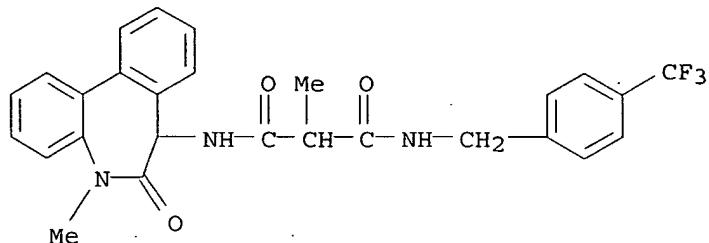
RN 741674-09-9 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(3-methoxyphenyl)methyl-2-methyl- (9CI) (CA INDEX NAME)



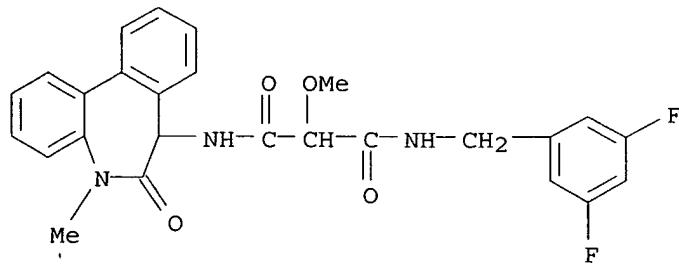
RN 741674-10-2 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(4-(trifluoromethyl)phenyl)methyl- (9CI) (CA INDEX NAME)



RN 741674-11-3 HCAPLUS

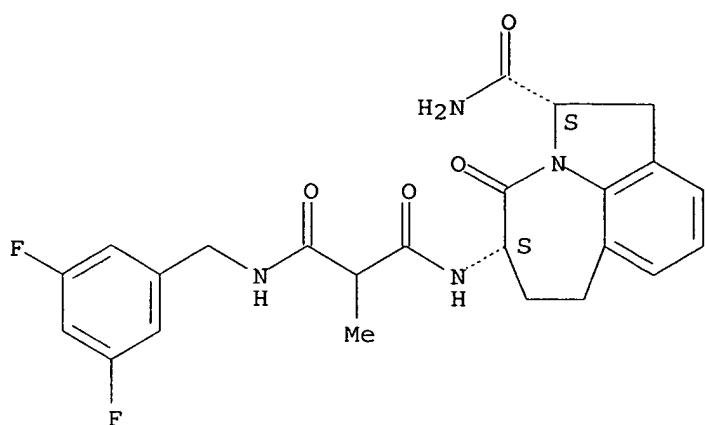
CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methoxy- (9CI) (CA INDEX NAME)



RN 741674-12-4 HCAPLUS

CN Propanediamide, N-[(2S,5S)-2-(aminocarbonyl)-1,2,4,5,6,7-hexahydro-4-oxoazepino[3,2,1-hi]indol-5-yl]-N'-(3,5-difluorophenyl)methyl)-2-methyl- (9CI) (CA INDEX NAME)

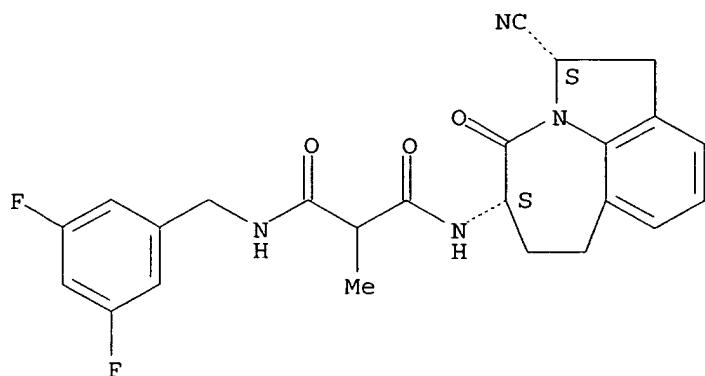
Absolute stereochemistry.



RN 741674-13-5 HCPLUS

CN Propanediamide, N-[(2S,5S)-2-cyano-1,2,4,5,6,7-hexahydro-4-oxoazepino[3,2,1-hi]indol-5-yl]-N'-(3,5-difluorophenyl)methyl]-2-methyl- (9CI) (CA INDEX NAME)

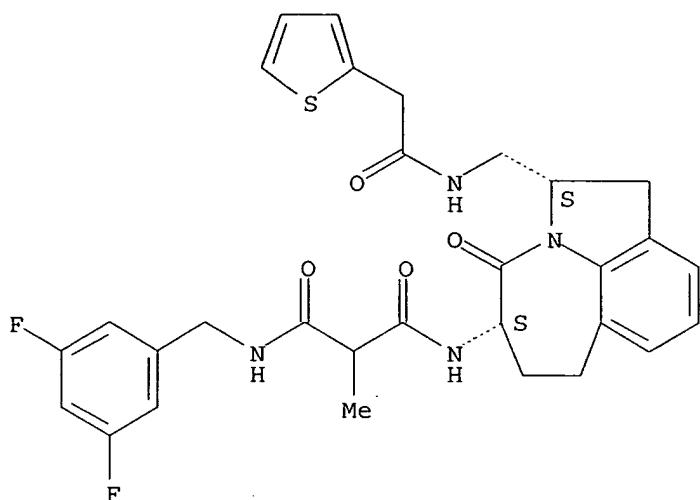
Absolute stereochemistry.



RN 741674-14-6 HCPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2S,5S)-1,2,4,5,6,7-hexahydro-4-oxo-2-[(2-thienylacetyl)amino]methyl]azepino[3,2,1-hi]indol-5-yl]-2-methyl- (9CI) (CA INDEX NAME)

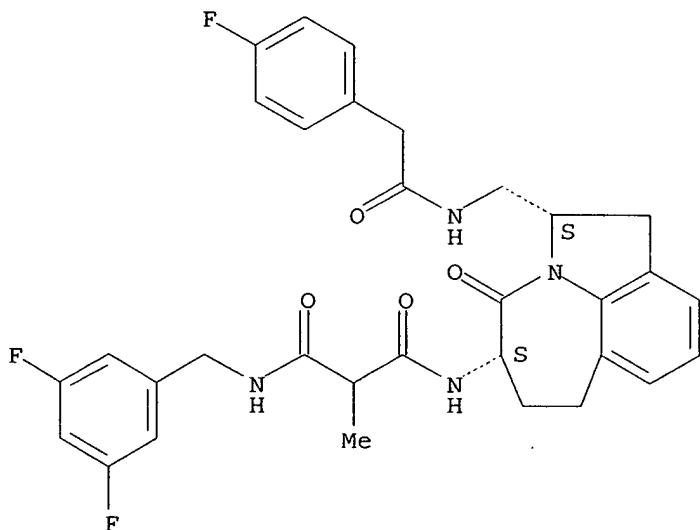
Absolute stereochemistry.



RN 741674-15-7 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2S,5S)-2-[(4-fluorophenyl)acetyl]amino]methyl]-1,2,4,5,6,7-hexahydro-4-oxoazepino[3,2,1-hi]indol-5-yl]-2-methyl- (9CI) (CA INDEX NAME)

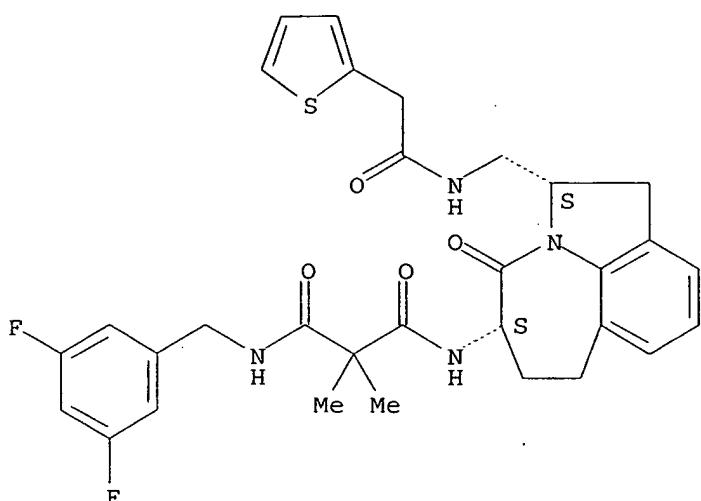
Absolute stereochemistry.



RN 741674-16-8 HCAPLUS

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2S,5S)-1,2,4,5,6,7-hexahydro-4-oxo-2-[(2-thienylacetyl)amino]methyl]azepino[3,2,1-hi]indol-5-yl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

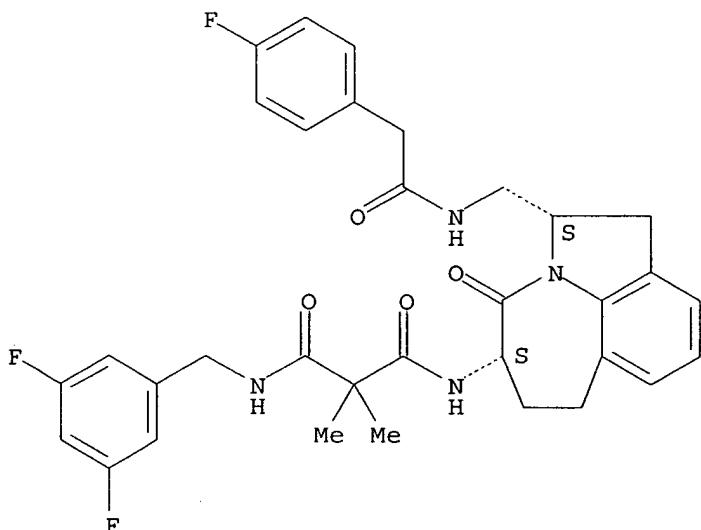
Absolute stereochemistry.



RN 741674-17-9 HCAPLUS

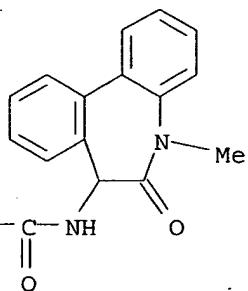
CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2S,5S)-2-[(4-fluorophenyl)acetyl]amino]methyl]-1,2,4,5,6,7-hexahydro-4-oxoazepino[3,2,1-hi]indol-5-yl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



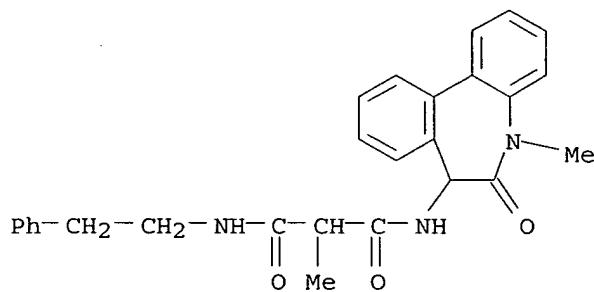
RN 741674-18-0 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-phenyl- (9CI) (CA INDEX NAME)



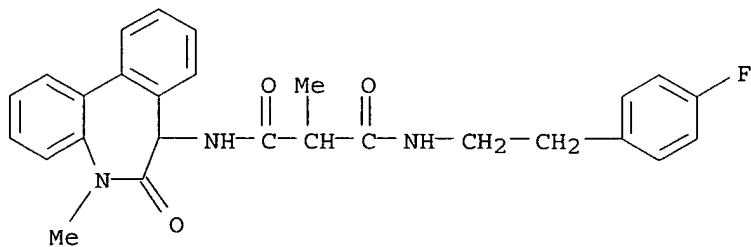
RN 741674-19-1 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2-phenylethyl)- (9CI) (CA INDEX NAME)



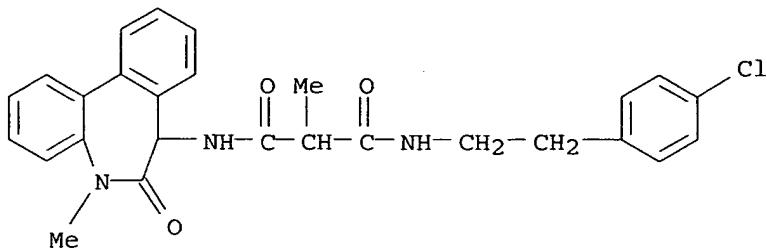
RN 741674-20-4 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-(4-fluorophenyl)ethyl)-2-methyl- (9CI) (CA INDEX NAME)



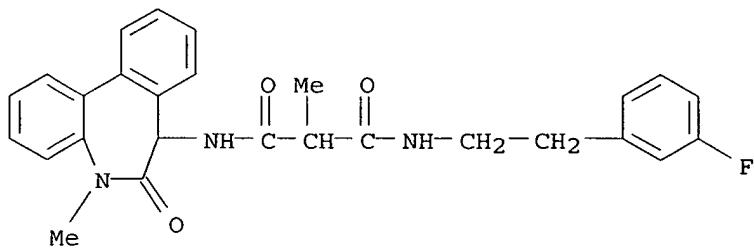
RN 741674-21-5 HCPLUS

CN Propanediamide, N-[2-(4-chlorophenyl)ethyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



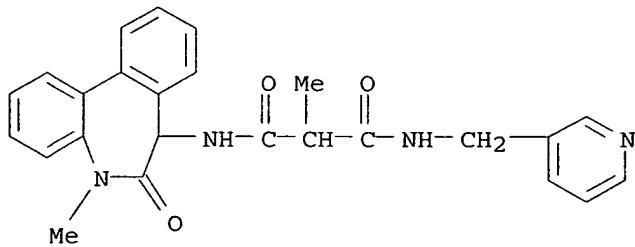
RN 741674-22-6 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-(3-fluorophenyl)ethyl)-2-methyl- (9CI) (CA INDEX NAME)



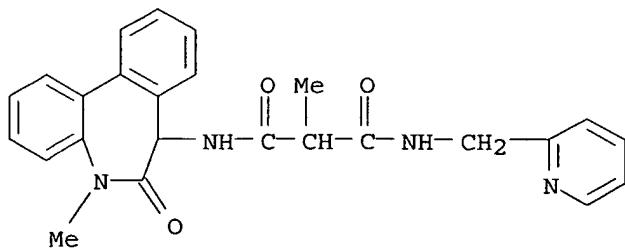
RN 741674-23-7 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



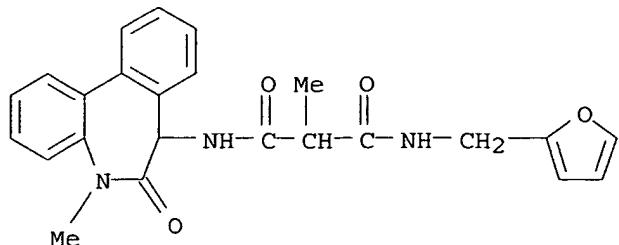
RN 741674-24-8 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



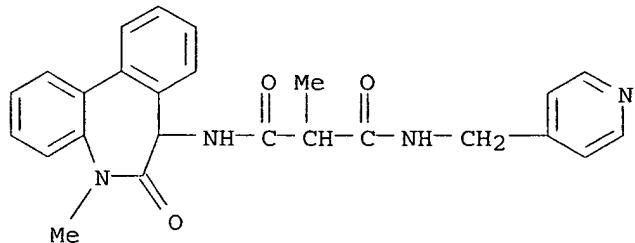
RN 741674-25-9 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(2-furanyl methyl)-2-methyl- (9CI) (CA INDEX NAME)



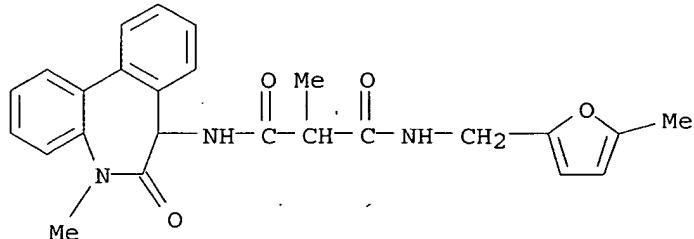
RN 741674-26-0 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



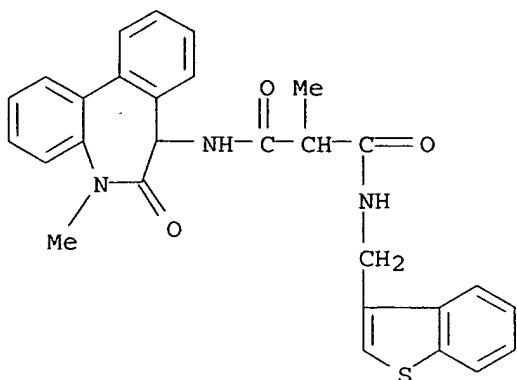
RN 741674-27-1 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(5-methyl-2-furanyl)methyl- (9CI) (CA INDEX NAME)



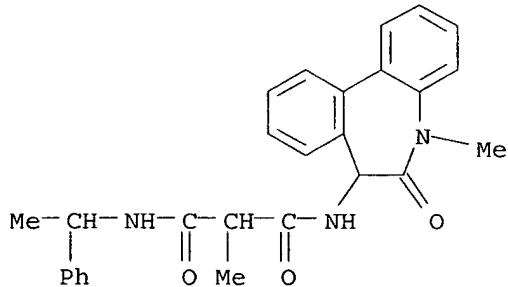
RN 741674-28-2 HCAPLUS

CN Propanediamide, N-(benzo[b]thien-3-ylmethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



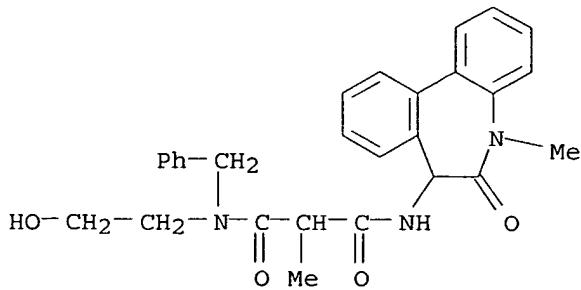
RN 741674-29-3 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(1-phenylethyl)- (9CI) (CA INDEX NAME)



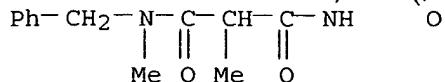
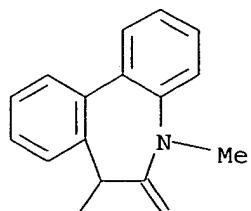
RN 741674-30-6 HCPLUS

CN Propanediamide, N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N-(2-hydroxyethyl)-2-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



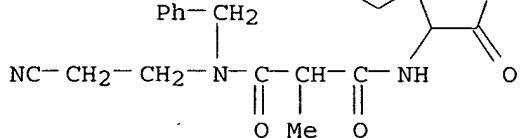
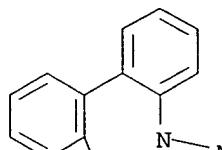
RN 741674-31-7 HCPLUS

CN Propanediamide, N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N,2-dimethyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



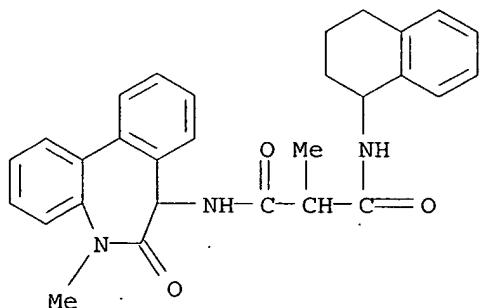
RN 741674-32-8 HCPLUS

CN Propanediamide, N-(2-cyanoethyl)-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



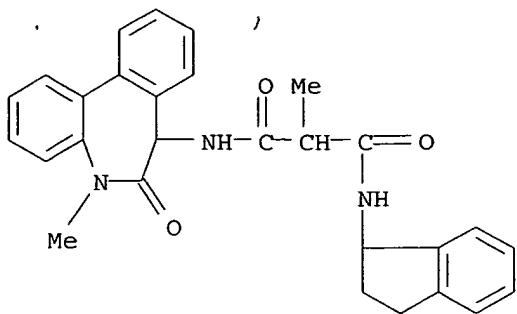
RN 741674-33-9 HCPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(1,2,3,4-tetrahydro-1-naphthalenyl)- (9CI) (CA INDEX NAME)



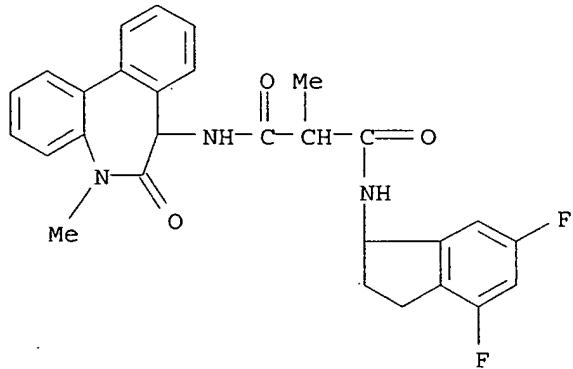
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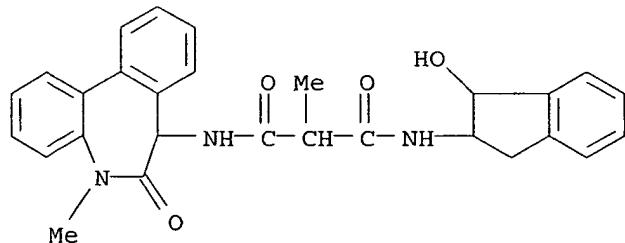
RN 741674-35-1 HCAPLUS

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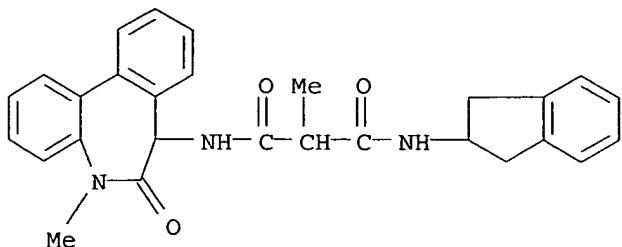
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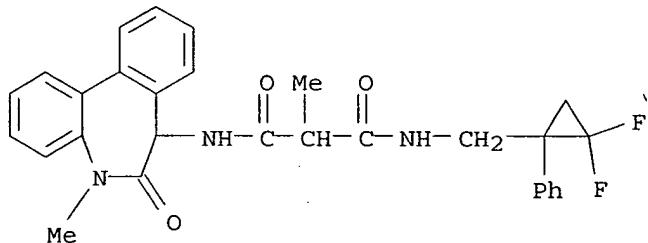
RN 741674-37-3 HCAPLUS

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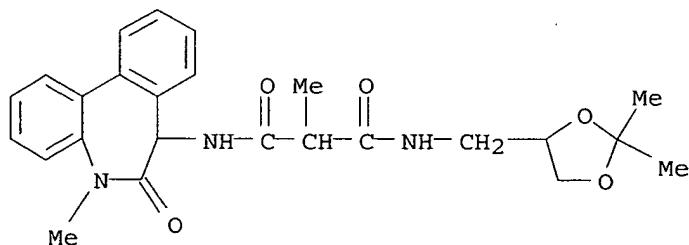
RN 741674-38-4 HCAPLUS

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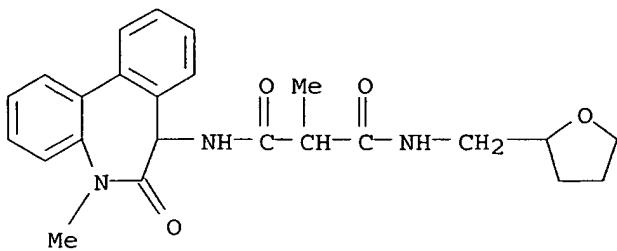
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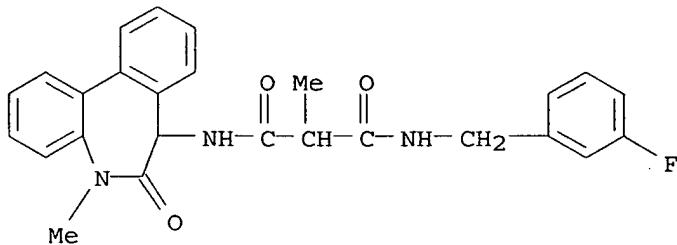
RN 741674-40-8 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(tetrahydro-2-furanyl)methyl- (9CI) (CA INDEX NAME)



RN 741674-99-7 HCAPLUS

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-N'-(3-fluorophenyl)methyl- (9CI) (CA INDEX NAME)



=> d ibib ab hitstr

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ACCESSION NUMBER: 2004:280921 USPATFULL

TITLE: Malonamide derivatives

INVENTOR(S): Galley, Guido, Rheinfelden, GERMANY, FEDERAL REPUBLIC

OF

Goergler, Annick, Colmar, FRANCE

Jacobsen, Helmut, Schopfheim, GERMANY, FEDERAL REPUBLIC
OF

Kitas, Eric Argirios, Aesch, SWITZERLAND

Peters, Jens-Uwe, Grenzach-Wyhlen, GERMANY, FEDERAL
REPUBLIC OF

NUMBER KIND DATE

PATENT INFORMATION: US 2004220222 A1 20041104

APPLICATION INFO.: US 2004-767784 A1 20040129 (10)

NUMBER DATE

PRIORITY INFORMATION: EP 2003-2190 20030204
 DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340
 KINGSLAND STREET, NUTLEY, NJ, 07110

NUMBER OF CLAIMS: 24
 EXEMPLARY CLAIM: 1
 LINE COUNT: 2424

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to malonamide derivatives of formula ##STR1##
 wherein ##STR2##

is a cyclic ring, selected from the group consisting of phenyl, pyridinyl, furanyl, benzo[b]thiophenyl, tetrahydronaphthyl, indanyl, 2,2-dimethyl-[1,3]dioxolanyl and tetrahydrofuranyl; ##STR3##

is selected from the group consisting of ##STR4##

and R.sup.1, R.sup.1', R.sup.2, R.sup.3, R.sup.11, R.sup.12, R.sup.13, R.sup.14, n and X are as defined in the specification and to pharmaceutically acceptable acid addition salts thereof. The compounds are γ -secretase inhibitors. Thus, the invention also relates to pharmaceutical compositions containing these compounds and to a method of treating Alzheimer's disease by administering the compounds of the invention.

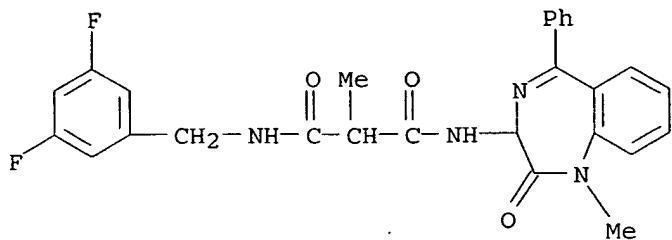
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 741674-40-8P 741674-99-7P

(preparation of malonamides and related compds. as γ -secretase inhibitors for the treatment of Alzheimer's disease.)

RN 741672-55-9 USPATFULL

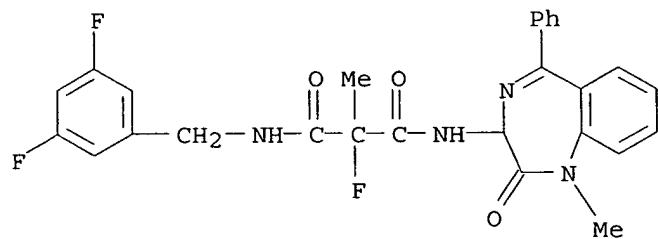
CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-

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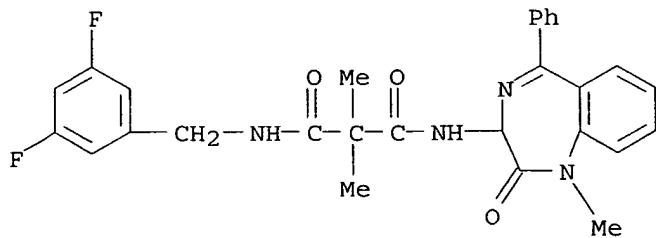
RN 741672-56-0 USPATFULL

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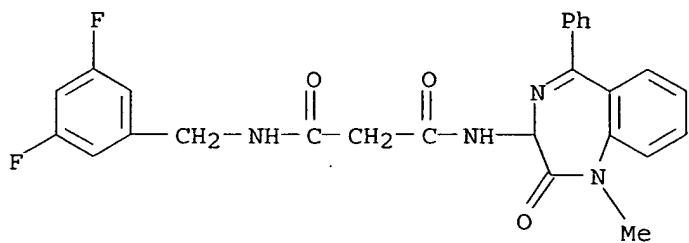
RN 741672-57-1 USPATFULL

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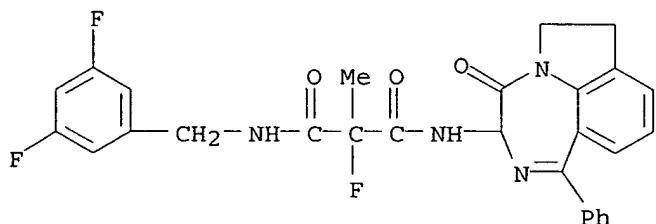
RN 741672-58-2 USPATFULL

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (9CI) (CA INDEX NAME)



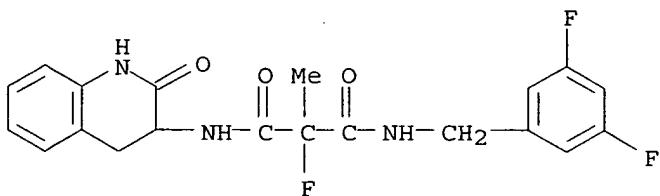
RN 741672-59-3 USPATFULL

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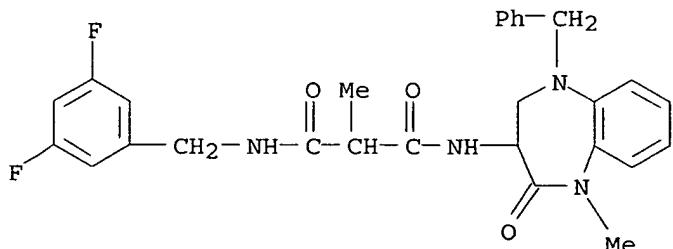
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-fluoro-2-methyl-N'-(1,2,3,4-tetrahydro-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)



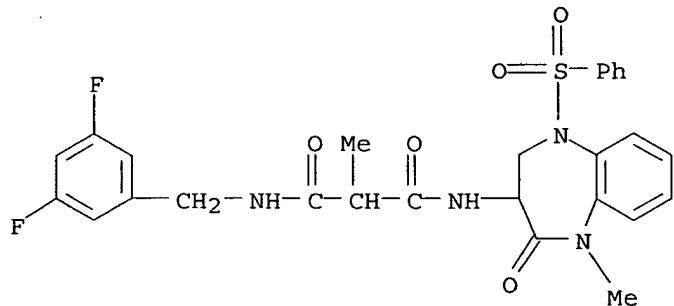
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-[2,3,4,5-tetrahydro-1-methyl-2-oxo-5-(phenylmethyl)-1H-1,5-benzodiazepin-3-yl]- (9CI) (CA INDEX NAME)



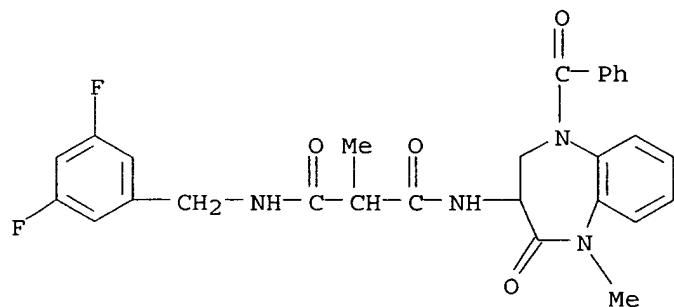
RN 741672-68-4 USPATFULL

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-2-methyl-N'-(2,3,4,5-tetrahydro-1-methyl-2-oxo-5-(phenylsulfonyl)-1H-1,5-benzodiazepin-3-yl)-(9CI) (CA INDEX NAME)



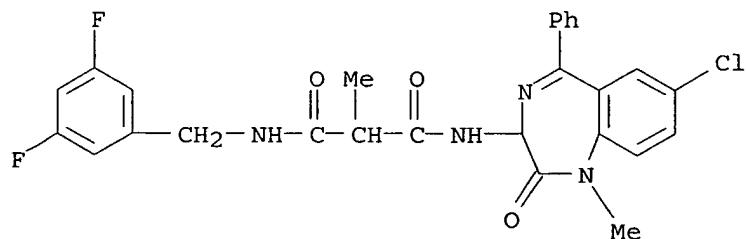
RN 741672-69-5 USPATFULL

CN Propanediamide, N-(5-benzoyl-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl)-N'-(3,5-difluorophenyl)methyl]-2-methyl-(9CI) (CA INDEX NAME)



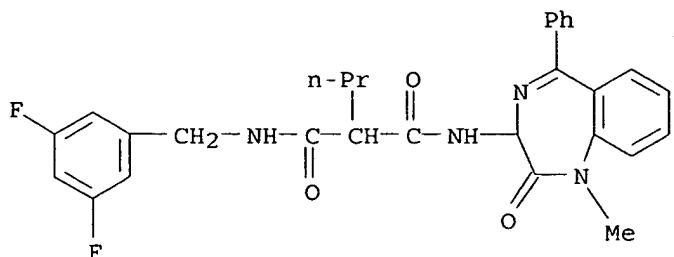
RN 741672-70-8 USPATFULL

CN Propanediamide, N-(7-chloro-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3,5-difluorophenyl)methyl]-2-methyl-(9CI) (CA INDEX NAME)

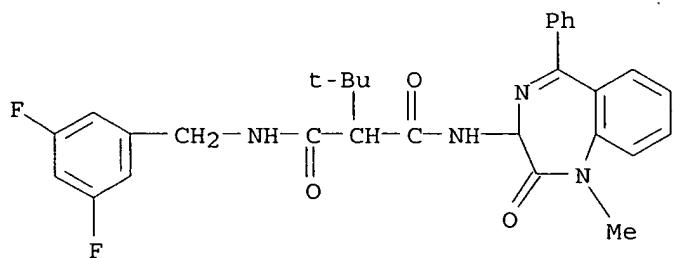


RN 741673-60-9 USPATFULL

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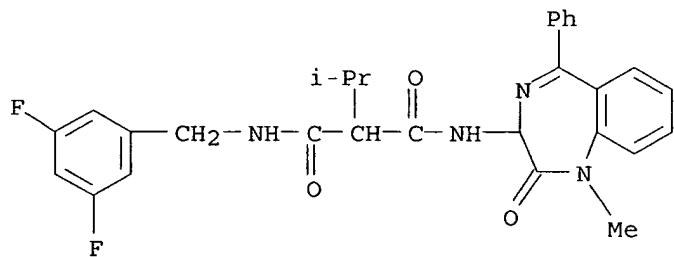


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(CA INDEX NAME)

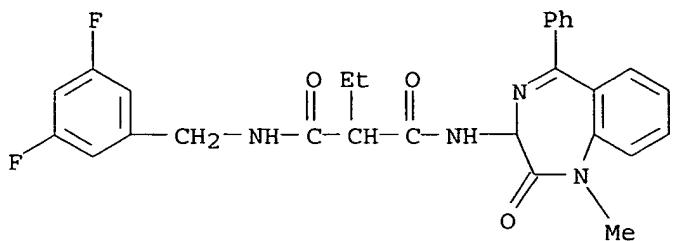
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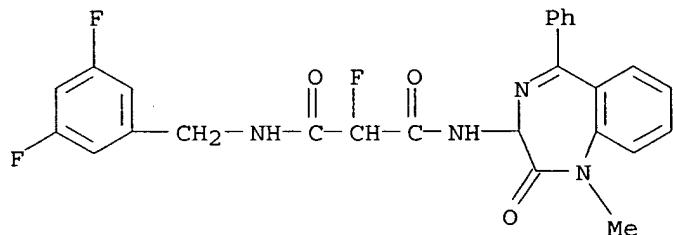
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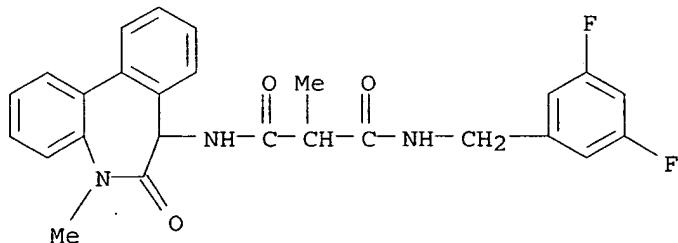
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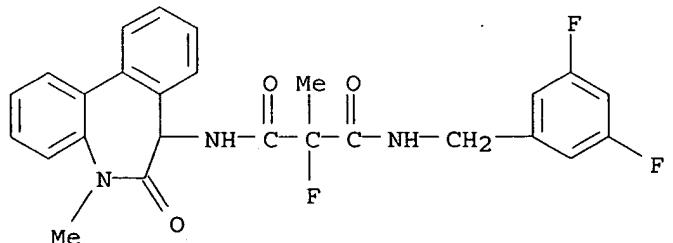
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CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



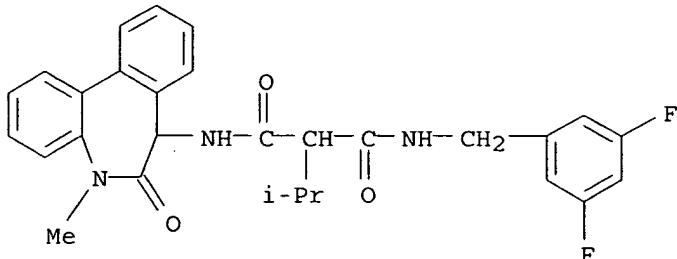
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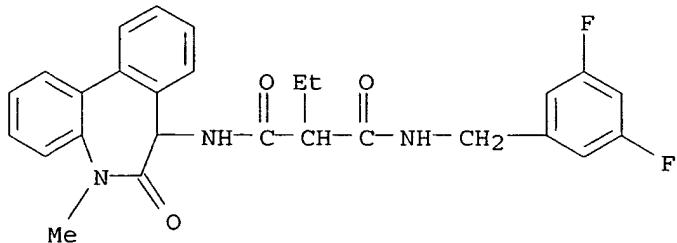
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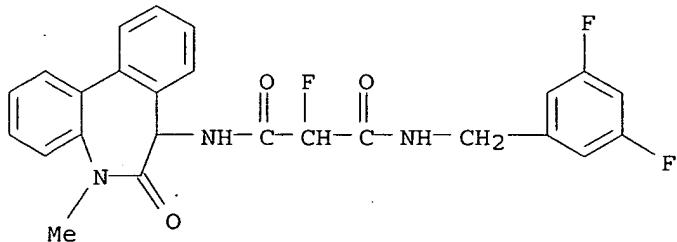
RN 741673-68-7 USPATFULL

CN Propanediamide, N-[(3,5-difluorophenyl)methyl]-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-ethyl- (9CI) (CA INDEX NAME)



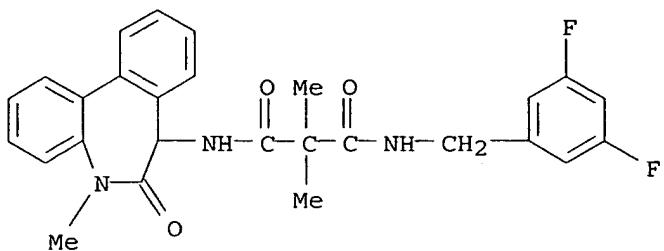
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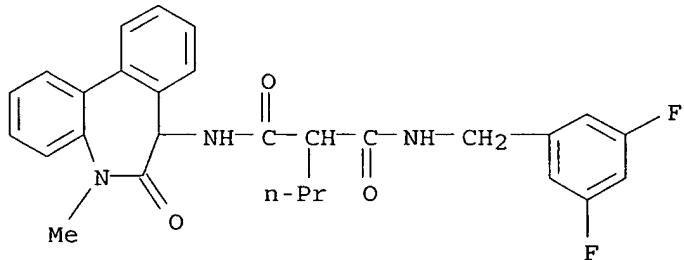
RN 741673-70-1 USPATFULL

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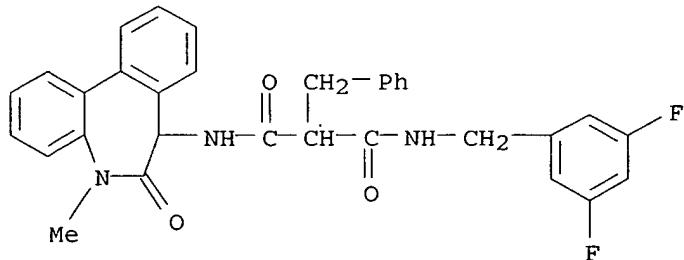
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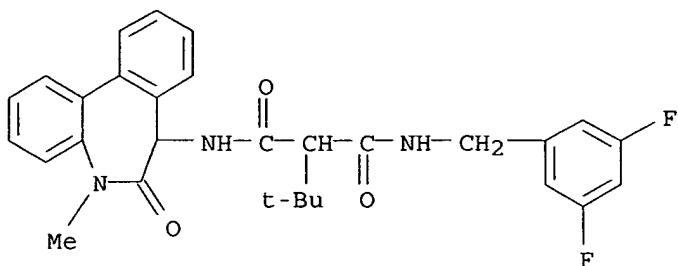
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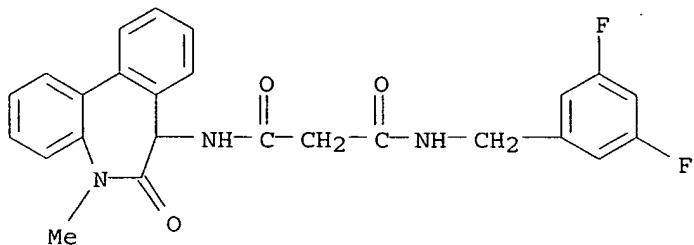
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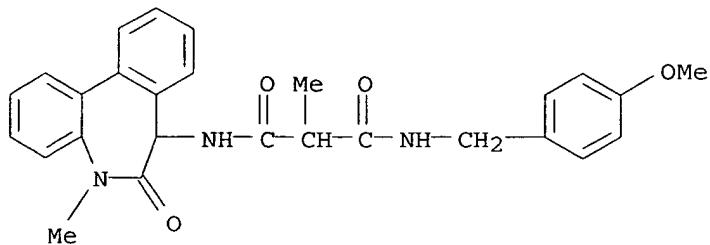
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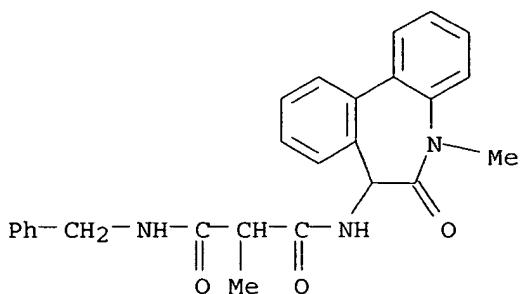
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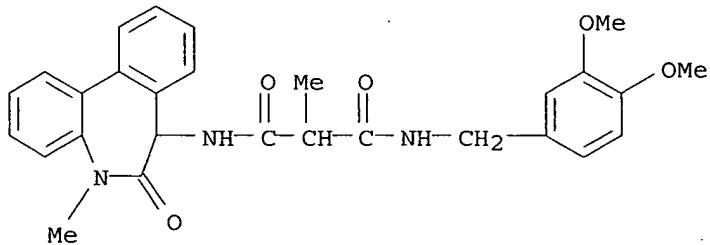
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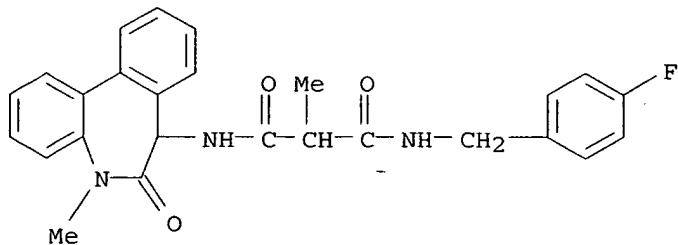
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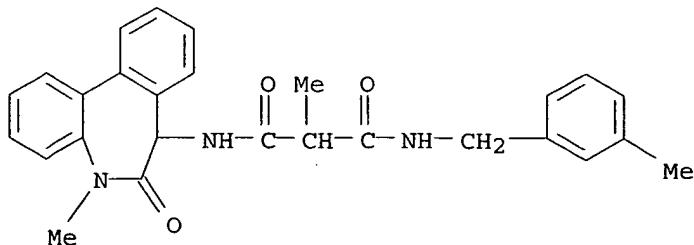
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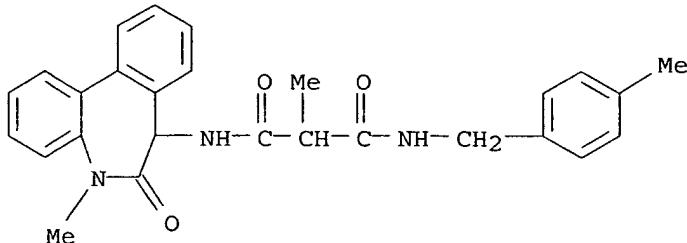
RN 741673-79-0 USPATFULL

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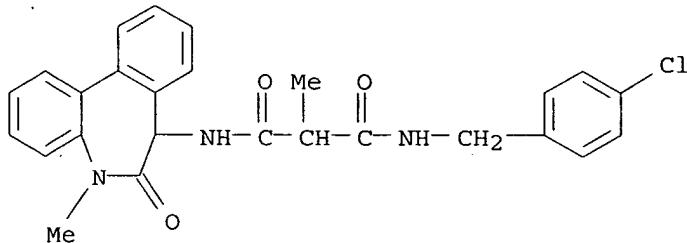
RN 741673-80-3 USPATFULL

CN Propanediamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl-N'-(4-methylphenyl)methyl- (9CI) (CA INDEX NAME)



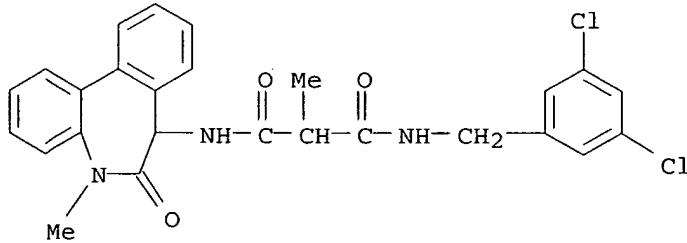
RN 741673-81-4 USPATFULL

CN Propanediamide, N-(4-chlorophenyl)methyl-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



RN 741673-82-5 USPATFULL

CN Propanediamide, N-(3,5-dichlorophenyl)methyl-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)



RN 741673-83-6 USPATFULL

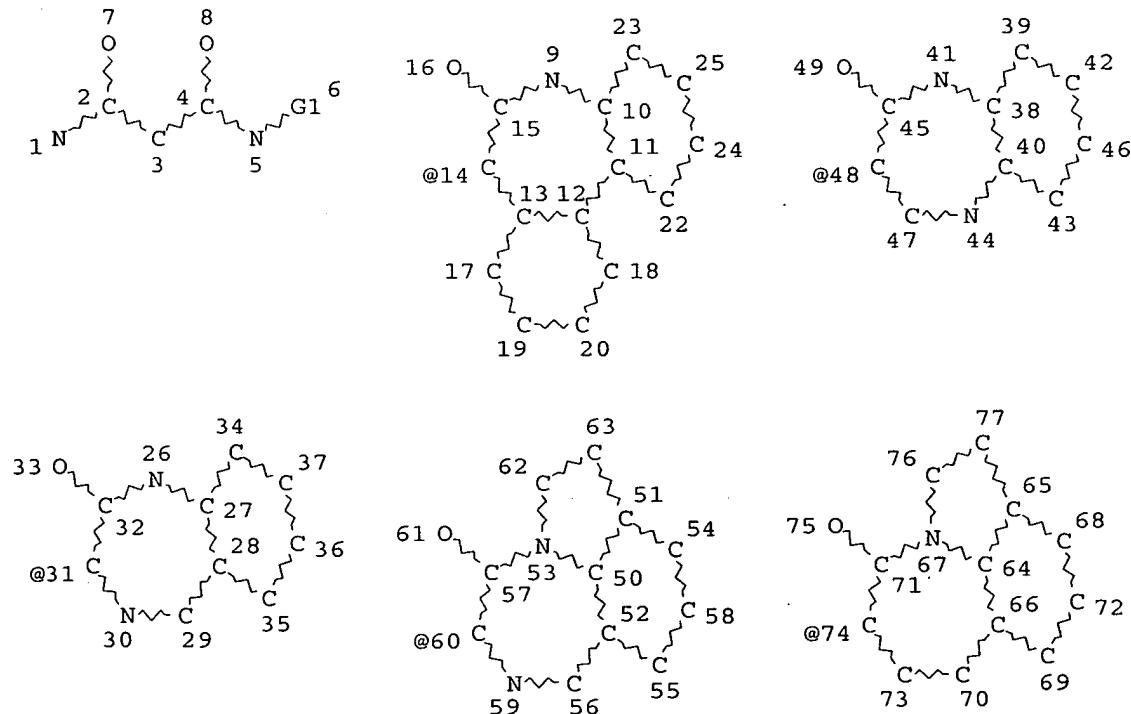
CN Propanediamide, N-(3-chlorophenyl)methyl-N'-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-2-methyl- (9CI) (CA INDEX NAME)

> d que 139

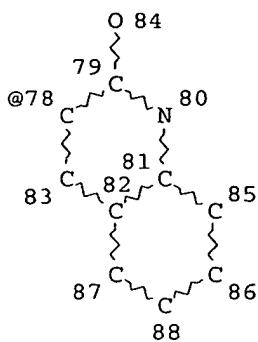
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 L12 QUE ABB=ON PLU=ON GOERGLER, A?/AU
 L13 QUE ABB=ON PLU=ON JACOBSEN, H?/AU
 L14 QUE ABB=ON PLU=ON KITAS, E?/AU
 L15 QUE ABB=ON PLU=ON ARGIRIOS, E?/AU
 L16 QUE ABB=ON PLU=ON PETERS, J?/AU
 L17 QUE ABB=ON PLU=ON PETERS, U?/AU
 L18 QUE ABB=ON PLU=ON (HOFFMAN OR (LA(W) ROCHE) OR LAROCHE)
 /PA,CS,SO
 L24 QUE ABB=ON PLU=ON ?AZEPIN?
 L25 QUE ABB=ON PLU=ON ?MALON?
 L26 3153 SEA FILE=HCAPLUS ABB=ON PLU=ON (L11 OR L12 OR L13 OR L14 OR
 L15 OR L16 OR L17)
 L27 34 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND (L24 OR L25)
 L28 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND ?MALONAMID?
 L29 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L18
 L31 17 SEA FILE=HCAPLUS ABB=ON PLU=ON (L27 OR L28 OR L29) AND
 (PHARM?/SC,SX)
 L37 QUE ABB=ON PLU=ON ?HYDROQUINOLIN? OR TETRAHYDROQUINOLI
 N? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
 L38 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND L37
 L39 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 OR L31

> d que 163

L6 STR



Page 1-A



Page 2-A

VAR G1=14/31/48/60/74/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 7
 CONNECT IS E1 RC AT 8
 CONNECT IS E1 RC AT 16
 CONNECT IS E1 RC AT 33
 CONNECT IS E1 RC AT 49
 CONNECT IS E1 RC AT 61
 CONNECT IS E1 RC AT 75
 CONNECT IS E1 RC AT 84
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 87

STEREO ATTRIBUTES: NONE

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 L43 QUE ABB=ON PLU=ON (A61K031-55 OR A61K031-551 OR A61K03
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 L46 QUE ABB=ON PLU=ON (D780 (P) J372)/M0,M1,M2,M3,M4,M5,M6
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 RAF81K/DCN OR RAF81L/DCN OR RAF81M/DCN OR RAF81N/DCN OR
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 RAH9OY/DCN OR RAH9OZ/DCN OR RAH901/DCN OR RAH903/DCN OR
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 RAH9P3/DCN OR RAH9P7/DCN OR RAH9P8/DCN OR RAH9P9/DCN)

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 N? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
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 L15 OR L16 OR L17)
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 L76 9 SEA FILE=MEDLINE ABB=ON PLU=ON L74 OR L75

=> d que 186

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 L25 QUE ABB=ON PLU=ON ?MALON?
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 N? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
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 L15 OR L16 OR L17)
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 L86 15 SEA FILE=EMBASE ABB=ON PLU=ON (L84 OR L85)

=> d his 193

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 BIOTECHNO, BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI,

DISSABS' ENTERED AT 12:29:41 ON 01 AUG 2006)
 L93 21 S L91 OR L92

=> d que 193

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L12	QUE ABB=ON PLU=ON	GOERGLER, A?/AU
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L14	QUE ABB=ON PLU=ON	KITAS, E?/AU
L15	QUE ABB=ON PLU=ON	ARGIRIOS, E?/AU
L16	QUE ABB=ON PLU=ON	PETERS, J?/AU
L17	QUE ABB=ON PLU=ON	PETERS, U?/AU
L24	QUE ABB=ON PLU=ON	?AZEPIN?
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L37	QUE ABB=ON PLU=ON	?HYDROQUINOLIN? OR TETRAHYDROQUINOLIN? N? OR ((HYDRO OR TETRAHYDRO) (2A) QUINOLIN?)
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L91	21 SEA L90 AND (L24 OR L37)	
L92	0 SEA L91 AND (L25 OR L40 OR L41)	
L93	21 SEA L91 OR L92	

=> dup rem 139 163 176 186 193

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PROCESSING COMPLETED FOR L39
 PROCESSING COMPLETED FOR L63
 PROCESSING COMPLETED FOR L76
 PROCESSING COMPLETED FOR L86
 PROCESSING COMPLETED FOR L93

L99 46 DUP REM L39 L63 L76 L86 L93 (27 DUPLICATES REMOVED)
 ANSWERS '1-17' FROM FILE HCAPLUS

ANSWERS '18-22' FROM FILE WPIX
 ANSWERS '23-28' FROM FILE MEDLINE
 ANSWERS '29-38' FROM FILE EMBASE
 ANSWERS '39-41' FROM FILE BIOSIS
 ANSWERS '42-43' FROM FILE PASCAL
 ANSWERS '44-46' FROM FILE SCISEARCH

=> file stnguide

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jul 28, 2006 (20060728/UP).

=> d ibib ed ab 1-46

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 SCISEARCH' - CONTINUE? (Y)/N:y

L99 ANSWER 1 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2005:29200 HCAPLUS
 DOCUMENT NUMBER: 142:134463
 TITLE: Preparation of 2-phenyl-N-(pyridin-3-yl)-N-methylisobutyramide derivatives as dual NK1/NK3 antagonists for treating schizophrenia
 INVENTOR(S): Hoffmann, Torsten; Koblet, Andreas; Peters, Jens-Uwe; Schnider, Patrick; Sleight, Andrew; Stadler, Heinz
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 374 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005002577	A1	20050113	WO 2004-EP6929	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004253267	A1	20050113	AU 2004-253267	20040625
CA 2530886	AA	20050113	CA 2004-2530886	20040625
EP 1643998	A1	20060412	EP 2004-740337	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2005090533	A1	20050428	US 2004-884707	20040702
NO 2005006007	A	20060119	NO 2005-6007	20051216

PRIORITY APPLN. INFO.: EP 2003-14513 A 20030703
 WO 2004-EP6929 W 20040625

OTHER SOURCE(S): MARPAT 142:134463

ED Entered STN: 13 Jan 2005

AB The invention is directed to the use of compds. of formula I [wherein R1 = (un)substituted aryl; R2, R3 = independently H, halo, alkyl, alkoxy, OCHF₂, OCH₂F, OCF₃, or CF₃; R4, R5 = independently H, CHO, (CH₂)_oS(O)p-alkyl, etc.; o = 0-3; p = 0-2; or R4NR5 form an (un)substituted ring with -(CH₂)₃₋₅-, -(CH₂)_{1,2,3-O-(CH₂)₂-}, -CH₂CH:CHCH₂-, etc.]; and their pharmaceutically active acid addition salts as dual neurokinin NK1/NK3 antagonists useful in the treatment of schizophrenia. The invention discloses 421 preps. of title compds. For example, II was prepared, in 2 steps, by acylation of N-[6-chloro-4-(2-chlorophenyl)pyridin-3-yl]methylamine (preparation given) with 2-(3,5-dichlorophenyl)-2-methylpropanoyl chloride (preparation given) and amination with (L)-prolinol. II bound to NK1 and NK3 receptors with pKi value of 8.47 and 9.05, resp.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 2005:303395 HCAPLUS
 DOCUMENT NUMBER: 142:373708
 TITLE: Preparation of carbamic acid alkyl ester derivatives as
 INVENTOR(S): Flohr, Alexander; Galley, Guido;
 Jakob-Roetne, Roland; Kitas, Eric Argirios;
 Peters, Jens-Uwe; Wostl, Wolfgang
 PATENT ASSIGNEE(S): Switz.
 SOURCE: U.S. Pat. Appl. Publ., 38 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005075327	A1	20050407	US 2004-951229	20040927
AU 2004283803	A1	20050506	AU 2004-283803	20040927
CA 2541470	AA	20050506	CA 2004-2541470	20040927
WO 2005040126	A1	20050506	WO 2004-EP10821	20040927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1673347	A1	20060628	EP 2004-787028	20040927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			EP 2003-22650	A 20031006
			WO 2004-EP10821	W 20040927

OTHER SOURCE(S): MARPAT 142:373708
 ED Entered STN: 08 Apr 2005

AB The compds. of general formula (I) and (II) [R1 = each (un)substituted -(CHR')q-aryl or -(CHR')q-heteroaryl, lower alkyl, lower alkenyl, -(CH2)nSiMe3, -(CH2)n-O-lower alkyl, -(CH2)n-S-lower alkyl, -(CH2)q-cycloalkyl, or -(CH2)n-[CH(OH)]m-(CF2)p-CHF(3-q), -(CH2)n-CR2-CF3 (wherein the two R radicals form together with the carbon atom a cycloalkyl ring); R' = H, lower alkyl; n = 1-3; m = 0, 1; p = 0-6; q = 0-3; R2 = H, lower alkyl; R3 = H, lower alkyl, -CH2CF2CF3, CH2CF3, (CH2)2CF3, CF3, CHF2, (un)substituted aryl, -(CH2)nNR5R6 (wherein R5, R6 = H, lower alkyl); R4 = Q, Q1 (wherein R7 = H, lower alkyl, -(CH2)nCF3, -(CH2)n-cycloalkyl); R8 = H, lower alkyl, -COPh, -C(O)-lower alkyl, -C(O)O-(CH2)n-cycloalkyl, -C(O)O-(CH2)n-lower alkyl, -C(O)NH-(CH2)n-lower alkyl, -C(O)NH-(CH2)n-cycloalkyl; R9 = H, lower alkyl, -(CH2)n-cycloalkyl, -(CH2)n-CF3] or pharmaceutically acceptable salts, optically pure enantiomers, racemates or diastereomeric mixts. thereof are prepared. These compds. inhibit amyloidogenic Abeta peptides, i.e. β -amyloid ($A\beta$) peptides, and are useful for the treatment of Alzheimer's disease. β -amyloid peptides. Thus, 0.12 g (0.25 mmol) carbonic acid 4-nitrophenyl ester (S)-1-((S)-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-ylcarbamoyl)ethyl ester and 543 μ l 2,2,3,3,3-pentafluoropropylamine were stirred at room temperature over night to give, after silica gel chromatog., 0.075 g (63%) (2,2,3,3,3-pentafluoropropyl)carbamic acid (1S)-1-[(7S)-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl]carbamoyl]ethyl ester (III). III showed IC50 of 0.001 μ M against γ -secretase.

L99 ANSWER 3 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2005:220131 HCPLUS

DOCUMENT NUMBER: 142:298014

TITLE: Preparation of dibenzoazepinylmalonamides, dibenzoazepinylmalonamides, benzodiazepinylmalonamides, and related compounds as γ -secretase inhibitors for treatment of Alzheimer's disease.

INVENTOR(S): Flohr, Alexander; Galley, Guido; Jakob-Roetne, Roland; Kitas, Eric Argirios; Peters, Jens-Uwe; Wostl, Wolfgang

PATENT ASSIGNEE(S): Switz.

SOURCE: U.S. Pat. Appl. Publ., 59 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005054633	A1	20050310	US 2004-933177	20040902
AU 2004270361	A1	20050317	AU 2004-270361	20040831
CA 2537440	AA	20050317	CA 2004-2537440	20040831
WO 2005023772	A1	20050317	WO 2004-EP9700	20040831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				

SN, TD, TG			
NO 2006001047	A 20060404	NO 2006-1047	20060303
PRIORITY APPLN. INFO.:		EP 2003-19683	A 20030909
		WO 2004-EP9700	W 20040831

OTHER SOURCE(S): MARPAT 142:298014
ED Entered STN: 13 Mar 2005
AB **Malonamides R1NHCOCR3R4CONHR2** [R1= Q1-Q4; R2 = alkyl, alkynyl, alkylthio, alkoxy(alkyl), halo(alkyl), etc.; R3, R4 = H, alkyl, alkoxy, Ph, halo; R5 = H, alkyl, trifluoromethyl(alkyl), cycloalkyl(alkyl); R6 = H, halo; R7 = H, alkyl; R8 = H, alkyl, alkynyl, trifluoromethyl(alkyl), cycloalkyl(alkyl), (halo-substituted) phenyl(alkyl); R9 = H, alkyl, CHO, alkylcarbonyl, F3CCO, (substituted) PhCO, etc.], were prepared Thus, 2-methyl-N-(5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl)malonamic acid (preparation given), cyclopropylmethylamine, and 2-(2-pyridon-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TPTU) were shaken together overnight in DMF to give N-cyclopropylmethyl-2-methyl-N'-(5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl)malonamide. The latter inhibited γ -secretase with IC₅₀ = 0.09 μ M.

L99 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2005:1182409 HCAPLUS
DOCUMENT NUMBER: 143:399661
TITLE: Fenobam: A clinically validated nonbenzodiazepine anxiolytic is a potent, selective, and noncompetitive mGlu5 receptor antagonist with inverse agonist activity
AUTHOR(S): Porter, Richard H. P.; Jaeschke, Georg; Spooren, Will; Ballard, Theresa M.; Buttelmann, Bernd; Kolczewski, Sabine; Peters, Jens-Uwe; Prinseen, Eric; Wichmann, Jurgen; Vieira, Eric; Muhlemann, Andreas; Gatti, Silvia; Mutel, Vincent; Malherbe, Pari
CORPORATE SOURCE: Pharma Division, Discovery Research CNS, F. Hoffmann-La Roche, Basel, Switz.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 315(2), 711-721
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Nov 2005
AB Fenobam [N-(3-chlorophenyl)-N'-(4,5-dihydro-1-methyl-4-oxo-1H-imidazole-2-yl)ureal] is an atypical anxiolytic agent with unknown mol. target that has previously been demonstrated both in rodents and human to exert anxiolytic activity. Here, we report that fenobam is a selective and potent metabotropic glutamate (mGlu)5 receptor antagonist acting at an allosteric modulatory site shared with 2-methyl-6-phenylethynyl-pyridine (MPEP), the prototypical selective mGlu5 receptor antagonist. Fenobam inhibited quisqualate-evoked intracellular calcium response mediated by human mGlu5 receptor with IC₅₀ = 58±2 nM. It acted in a noncompetitive manner, similar to MPEP and demonstrated inverse agonist properties, blocking 66% of the mGlu5 receptor basal activity (in an over expressed cell line) with an IC₅₀ = 84±13 nM. [³H]Fenobam bound to rat and human recombinant receptors with K_d values of 54±6 and 31±4 nM, resp. MPEP inhibited [³H]fenobam binding to human mGlu5 receptors with a K_i value of 6.7±0.7 nM, indicating a common binding site shared by both allosteric antagonists. Fenobam exhibits anxiolytic activity in the stress-induced hyperthermia model, Vogel conflict test, Geller-Seifter conflict test, and conditioned emotional response with a min. ED of 10 to 30 mg/kg p.o.

Furthermore, fenobam is devoid of GABAergic activity, confirming previous reports that fenobam acts by a mechanism distinct from benzodiazepines. The non-GABAergic activity of fenobam, coupled with its robust anxiolytic activity and reported efficacy in human in a double blind placebo-controlled trial, supports the potential of developing mGlu5 receptor antagonists with an improved therapeutic window over benzodiazepines as novel anxiolytic agents.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 5 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2004:675740 HCPLUS

DOCUMENT NUMBER: 141:206827

TITLE: Preparation of malonamides and related compounds as γ -secretase inhibitors for the treatment of Alzheimer's disease.

INVENTOR(S): Galley, Guido; Goergler, Annick; Jacobsen, Helmut; Kitas, Eric Argirios; Peters, Jens-Uwe

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069826	A1	20040819	WO 2004-EP674	20040127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004210036	A1	20040819	AU 2004-210036	20040127
CA 2514267	AA	20040819	CA 2004-2514267	20040127
EP 1592684	A1	20051109	EP 2004-705404	20040127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007262	A	20060131	BR 2004-7262	20040127
CN 1745076	A	20060308	CN 2004-80003305	20040127
JP 2006516556	T2	20060706	JP 2006-500017	20040127
US 2004220222	A1	20041104	US 2004-767784	20040129
NO 2005003627	A	20050810	NO 2005-3627	20050726
PRIORITY APPLN. INFO.:			EP 2003-2190	A 20030204
			WO 2004-EP674	W 20040127

OTHER SOURCE(S): MARPAT 141:206827

ED Entered STN: 19 Aug 2004

AB Title compds. I [L = bond, (CH₂)₁₋₂, CH(CH₃), etc.; C = cyclic ring, e.g., Ph, pyridinyl, furanyl, etc.; X = (R₂)_{1,2,3}; (R₂)_{1,2,3} = H, OH, halo, etc.; R₁, R_{1'} = H, alkyl, halo, etc.; R₁₄ = H, alkyl, (CH₂)₂OH, etc.; A = substituted 5,7-dihydro-6H-dibenz[b,d]azepin-6-ones, 1,3-dihydro-5-phenyl-1,4-benzodiazepin-2-ones, 3,4-dihydro-2-quinolinones, etc.] and their pharmaceutically acceptable salts and formulations were prepared. For example, coupling of 3-amino-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one

and malonamic acid II, e.g., prepared from di-Et Me malonate in 3-steps, afforded malonamide III in 67% yield. In γ -secretase inhibition assays, 37-examples of compds. I exhibited IC₅₀ values ranging from 0.003-0.11 μ M, the IC₅₀ value of malonamide III was 0.83 μ M. Compds. I are claimed useful for the treatment of Alzheimer's disease.

L99 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
 ACCESSION NUMBER: 2003:656755 HCAPLUS
 DOCUMENT NUMBER: 139:197497
 TITLE: Preparation of novel pyridines and pyrimidines as DPP IV inhibitors
 INVENTOR(S): Boehringer, Markus; Loeffler, Bernd Michael;
 Peters, Jens-Uwe; Steger, Matthias; Weiss, Peter
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 73 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068757	A1	20030821	WO 2003-EP1107	20030205
WO 2003068757	C2	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2474578	AA	20030821	CA 2003-2474578	20030205
AU 2003206833	A1	20030904	AU 2003-206833	20030205
EP 1476435	A1	20041117	EP 2003-704536	20030205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007665	A	20050104	BR 2003-7665	20030205
CN 1630644	A	20050622	CN 2003-803774	20030205
JP 2005526035	T2	20050902	JP 2003-567888	20030205
US 2003216382	A1	20031120	US 2003-361268	20030210
US 6867205	B2	20050315		
US 2005143405	A1	20050630	US 2005-37989	20050118
US 7022718	B2	20060404		
PRIORITY APPLN. INFO.:				
		EP 2002-3114	A 20020213	
		WO 2003-EP1107	W 20030205	
		US 2003-361268	A3 20030210	

OTHER SOURCE(S): MARPAT 139:197497

ED Entered STN: 22 Aug 2003

AB The title compds. [I; X = N, CR₅; R₁, R₂ = H, alkyl; R₃ = (un)substituted heterocyclyl or aryl; R₄ = alkyl, alkoxy, alkylthio, etc.; R₅ = H, alkyl], useful for the treatment and/or prophylaxis of diseases which are associated with DPP IV, such as diabetes, particularly non-insulin dependent diabetes mellitus, and impaired glucose tolerance, were prepared and formulated. Thus, reacting benzamidine with 2-(2,4-dimethylbenzylidene)

malononitrile in the presence of K₂CO₃ in MeOH followed by treating the reaction residue with KMnO₄ in Me₂CO, and reduction of the resulting nitrile with LiAlH₄ in THF afforded 7% II which showed IC₅₀ of 0.172 μM against DPP IV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 7 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2003:656747 HCPLUS

DOCUMENT NUMBER: 139:197384

TITLE: Preparation of novel pyridine and quinoline derivatives as DPP IV inhibitors

INVENTOR(S): Boehringer, Markus; Loeffler, Bernd Michael; Peters, Jens-Uwe; Riemer, Claus; Weiss, Peter

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068748	A1	20030821	WO 2003-EP1112	20030205
WO 2003068748	C2	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2474460	AA	20030821	CA 2003-2474460	20030205
AU 2003206834	A1	20030904	AU 2003-206834	20030205
EP 1476429	A1	20041117	EP 2003-704539	20030205
EP 1476429	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007576	A	20050111	BR 2003-7576	20030205
CN 1630639	A	20050622	CN 2003-803775	20030205
JP 2005526034	T2	20050902	JP 2003-567879	20030205
AT 309988	E	20051215	AT 2003-704539	20030205
ES 2252656	T3	20060516	ES 2003-3704539	20030205
US 2003195188	A1	20031016	US 2003-364490	20030211
US 6800650	B2	20041005		
PRIORITY APPLN. INFO.:			EP 2002-3115	A 20020213
			WO 2003-EP1112	W 20030205

OTHER SOURCE(S): MARPAT 139:197384

ED Entered STN: 22 Aug 2003

AB The title compds. [I; R₁ = H, alkyl; R₂ = (un)substituted heterocycl, aryl; R₃ and R₄ together with the carbon atoms to which they are attached form (un)substituted Ph or 5-7 membered saturated ring which may optionally contain a heteroatom selected from O, N and S, and the said saturated ring being ortho-fused to 5-6 membered aryl or heteroaryl], useful for the treatment and/or prophylaxis of diseases which are associated with DPP IV, such as diabetes, particularly non-insulin dependent diabetes mellitus,

and impaired glucose tolerance, were prepared and formulated. Thus, reacting 2-(2,4-dichlorobenzylidene)malononitrile with chroman-4-one in the presence of AcONH₄ in PhMe followed by reduction of the intermediate with LiAlH₄ in THF afforded 7% II which showed IC₅₀ of 0.018 μM against DPP IV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 8 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 1999:458726 HCPLUS

DOCUMENT NUMBER: 131:125287

TITLE: Flumazenil in children after esophagogastroduodenoscopy

AUTHOR(S): Peters, John M.; Tolia, Vasu; Simpson, Pippa; Aravind, Manaphanath K.; Kauffman, Ralph E.

CORPORATE SOURCE: Divisions of Pediatric Gastroenterology and Clinical Pharmacology, Wayne State University School of Medicine, Detroit, MI, USA

SOURCE: American Journal of Gastroenterology (1999), 94(7), 1857-1861

CODEN: AJGAAR; ISSN: 0002-9270

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 27 Jul 1999

AB OBJECTIVE: Our aim was to evaluate if the routine use of the benzodiazepine antagonist flumazenil would shorten post-procedure recovery times after esophagogastroduodenoscopy in pediatric patients receiving standard i.v. conscious sedation with the benzodiazepine diazepam in combination with meperidine. METHODS: Upper endoscopy was performed using i.v. conscious sedation with standardized doses of diazepam and meperidine on 29 children, age range 6-18 yr. Patients were randomized in a double-blind fashion to receive either i.v. normal saline (placebo) or 0.01 mg/kg (maximum, 1.0 mg) flumazenil within 5 min of procedure completion. Evaluation of the degree of sedation using a modified Observer's Assessment of Alertness/Sedation Scale was performed presedation, immediately before reversal solution administration, and serially over 60 min after reversal solution injection. RESULTS: Fifteen patients received flumazenil and 14 received placebo; patient group composition did not vary significantly in age and weight. Fifty-four percent of flumazenil patients and 30% of control patients achieved full alertness within 10 min of reversal solution injection. However, this difference between groups was not significant ($p > 0.45$). Resedation or side effects directly attributable to flumazenil were not observed. CONCLUSIONS: A single postsedation dose of flumazenil is well-tolerated in children >6 yr old. However, its routine use after esophagogastroduodenoscopy is of questionable benefit in shortening recovery time in this age group.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 9 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1994:188768 HCPLUS

DOCUMENT NUMBER: 120:188768

TITLE: CSF diazepam binding inhibitor and schizophrenia: clinical and biochemical relationships

AUTHOR(S): van Kammen, Daniel P.; Guidotti, Alessandro; Kelley, Mary E.; Gurkis, John; Guarneri, Patrizia; Gilbertson, Mark W.; Yao, Jeffrey K.; Peters, Jeffrey; Costa, Erminio

CORPORATE SOURCE: VAMC, Pittsburgh, PA, USA

SOURCE: Biological Psychiatry (1993), 34(8), 515-22
 CODEN: BIPCBF; ISSN: 0006-3223

DOCUMENT TYPE: Journal
 LANGUAGE: English

ED Entered STN: 16 Apr 1994

AB Diazepam-binding inhibitor (DBI) is a 9-kD neuropeptide that interacts with the benzodiazepine (BZD) binding sites of the neuronal γ -aminobutyric acid type A (GABA_A) receptor and with the glial mitochondrial BZD receptor (MBR). The authors explored the involvement of CSF DBI-LI in schizophrenia, based on the potential role of GABA in the neg. symptoms associated with schizophrenia, the relationship of its receptors with dopamine and norepinephrine release, and the proposed therapeutic efficacy of BZDs in schizophrenia. Clin. data, CSF DBI-LI and CSF monoamine measures were obtained in 65 drug-free male chronic (DSM-IIIR) schizophrenic patients, 53 of whom were also tested prior to haloperidol withdrawal. Following haloperidol withdrawal, CSF DBI-LI increased significantly. Drug-free CSF DBI-LI did not correlate with CSF monoamines. CSF DBI-LI was significantly higher in paranoid compared to chronic undifferentiated schizophrenic patients. The data suggest that DBI may have a symptom modulatory rather than an etiol. role in schizophrenia.

L99 ANSWER 10 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:53048 HCPLUS

DOCUMENT NUMBER: 144:128869

TITLE: Preparation of N-(2-oxoazepan-3-yl)sulfonamides as γ -secretase inhibitors for treating Alzheimer's disease and cancers

INVENTOR(S): Galley, Guido; Kitas, Eric, Argirios;
 ; Jakob-Roetne, Roland

PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.

SOURCE: PCT Int. Appl., 107 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006005486	A1	20060119	WO 2005-EP7268	20050706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006014945	A1	20060119	US 2005-179703	20050712
PRIORITY APPLN. INFO.:			EP 2004-103339	A 20040713

OTHER SOURCE(S): MARPAT 144:128869

ED Entered STN: 20 Jan 2006

AB Title compds. I [R₁ = (un)substituted hetero/aryl; R₂-R₄, R_{2'}-R_{4'} = H, lower alkyl, Ph or lower alkyl substituted by halogen; R₅ = cycloalkyl, (un)substituted hetero/aryl; X = CHR; R = H, lower alkyl; and their

pharmaceutically suitable acid addition salts, optical pure enantiomers, racemates or diastereomeric] were prepared as γ -secretase inhibitors. Thus, reductive amination of 3-fluoro-p-anisaldehyde with 3-aminoazepan-2-one and reaction with 5-chlorothiophene-2-sulfonyl chloride gave sulfonamide II. Preferred I inhibited γ -secretase with IC₅₀ < 0.3 μ M. I are useful in the treatment of Alzheimer's disease or common cancers.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 11 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:1019771 HCPLUS
 DOCUMENT NUMBER: 142:6564
 TITLE: Preparation of 1,4-benzoxazepin-3-ones as inhibitors of γ -secretase for the treatment of Alzheimer's disease
 INVENTOR(S): Galley, Guido; Goodnow, Robert Alan;
 Peters, Jens-Uwe
 PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004235819	A1	20041125	US 2004-838054	20040503
US 7060698	B2	20060613		
AU 2004238037	A1	20041125	AU 2004-238037	20040514
CA 2524640	AA	20041125	CA 2004-2524640	20040514
WO 2004100958	A1	20041125	WO 2004-EP5177	20040514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631296	A1	20060308	EP 2004-732944	20040514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1794997	A	20060628	CN 2004-80014015	20040514
BR 2004010647	A	20060704	BR 2004-10647	20040514
PRIORITY APPLN. INFO.:			EP 2003-11040	A 20030519
			WO 2004-EP5177	W 20040514

OTHER SOURCE(S): MARPAT 142:6564

ED Entered STN: 26 Nov 2004

AB 1,4-Benzoxazepin-3-ones I [m = 0-2; n = 1, 2; p = 1, 2; R1 = H, halogen, alkoxy, amino, alkylamino, dialkylamino; R2 = H, alkyl, cycloalkyl-(CH₂)_m, Ph(CH₂)_m, alkoxy-(CH₂)_m; R3 = alkyl, alkoxycarbonyl-(CH₂)_m, Ph(CH₂)_m, cycloalkyl; R4 = (un)substituted Ph(CH₂)_p, cycloalkyl, tetrahydronaphthalen-1-yl, 9-fluorenyl, alkyl] such as II are prepared as γ -secretase inhibitors for the treatment of Alzheimer's disease. Treatment of 5-bromosalicylaldehyde with base

followed by addition of Et 2-bromo-3-methylbutyrate yields Et 2-(4-bromo-2-formylphenoxy)-3-methylbutanoate, which is hydrolyzed to yield 2-(4-bromo-2-formylphenoxy)-3-methylbutanoic acid (III); stirring III with 2,6-difluorobenzylamine and cyclohexyl isocyanide in DMSO yields II. IC₅₀ values (without units) are given for the inhibition of γ -secretase by some of the title compds. E.g., II inhibits γ -secretase with an IC₅₀ value of 0.28 (no units given). A process for the preparation of the title compds. using a cyclocondensation of (formylaryloxy)alkanoic acids, amines, and isonitriles is claimed.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 12 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:465516 HCPLUS
 DOCUMENT NUMBER: 141:190752
 TITLE: An aminomethylpyrimidine DPP-IV inhibitor with improved properties
 AUTHOR(S): Peters, Jens-Uwe; Hunziker, Daniel; Fischer, Holger; Kansy, Manfred; Weber, Silja; Kritter, Stephane; Muller, Aranka; Wallier, Angelina; Ricklin, Fabienne; Boehringer, Markus; Poli, Sonia Maria; Csato, Miklos; Loeffler, Bernd-Michael
 CORPORATE SOURCE: Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd, Basel, CH-4070, Switz.
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(13), 3575-3578
 CODEN: BMCL8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:190752
 ED Entered STN: 10 Jun 2004
 AB A recently identified dipeptidyl peptidase IV (DPP-IV) inhibitor I (R = Ph) was found to induce phospholipidosis and to inhibit CYP3A4. A small series of less lipophilic and less amphiphilic analogs I (R = Me, MeO, H₂N, EtNMe, 4-morpholinyl, 1-azetidinyl, etc.) was synthesized in an effort to overcome these issues. I (R = MeOCH₂CH₂NMe) was equipotent to I (R = Ph), did not induce phospholipidosis and showed a reduced CYP3A4 inhibition.
 REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 13 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:904170 HCPLUS
 DOCUMENT NUMBER: 136:37519
 TITLE: Synthesis and use of triazaspirodecanone derivatives as neurokinin receptor antagonists
 INVENTOR(S): Galley, Guido; Godel, Thierry; Goergler, Annick; Hoffmann, Torsten; Kolczewski, Sabine; Roever, Stephan
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
 SOURCE: PCT Int. Appl., 90 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001094346	A1	20011213	WO 2001-EP6305	20010601
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002006932	A1	20020117	US 2001-861795	20010521
US 6482829	B2	20021119		
CA 2411716	AA	20011213	CA 2001-2411716	20010601
EP 1292596	A1	20030319	EP 2001-945242	20010601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011538	A	20030701	BR 2001-11538	20010601
JP 2003535863	T2	20031202	JP 2002-501895	20010601
ZA 2002009488	A	20040223	ZA 2002-9488	20021121
PRIORITY APPLN. INFO.:			EP 2000-112285	A 20000608
			WO 2001-EP6305	W 20010601

OTHER SOURCE(S): MARPAT 136:37519

ED Entered STN: 14 Dec 2001

AB Title compds. I [R1 = H, alkyl, alkenyl, Ph, (CH₂)_m-non aromatic heterocyclyl, (CH₂)_m-heteroaryl, (CH₂)_m-carboxamide, (CH₂)_m-C(O)alkyl, etc.; R2 = H, alkyl, halo, alkoxy; R3 = alkyl, alkoxy, halo, CF₃; X = N-, C:, CH; X₁/X₂ = H, OH, alkoxy or may be together an oxo group; Y₁/Y₂ = H, alkyl, (CH₂)_m-Ph or may be together an oxo group; Z = bond, CH₂, C(O); m = 0 - 4; n = 2 - 3; p = 0 - 2] were prepared Over 160 synthetic examples were disclosed. For example, 8-(3,5-bistrifluoromethylbenzoyl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one was reacted with 2-chloro-4,6-dimethoxy-1,3,5-triazine (1,2-dimethoxyethane, NaH, 100°C, 1 h) to give II. II had pKi = 8.66 for the NK-1 receptor. I are useful in the treatment of diseases related to NK-1 receptor antagonists.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 14 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:161079 HCPLUS

DOCUMENT NUMBER: 128:217636

TITLE: Preparation of peptidyl thrombin inhibitors.

INVENTOR(S): Van Boeckel, Constant Adriaan Anton; Adang, Anton Egbert Peter; Peters, Jacobus Albertus Maria

PATENT ASSIGNEE(S): AKzo Nobel N.V., Neth.

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXxd2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807308	A2	19980226	WO 1997-EP4579	19970819
WO 9807308	A3	20000824		
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9707209	A	19980220	ZA 1997-7209	19970812
AU 9746181	A1	19980306	AU 1997-46181	19970819
EP 956293	A1	19991117	EP 1997-944781	19970819

EP 956293	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 282629	E	20041215	AT 1997-944781	19970819
TW 515803	B	20030101	TW 1997-86112645	19970830
PRIORITY APPLN. INFO.:			EP 1996-202336	A 19960823
			WO 1997-EP4579	W 19970819

OTHER SOURCE(S): MARPAT 128:217636

ED Entered STN: 18 Mar 1998

AB Title compds. of formula R1R2NCH(R3)CO-A-B-X and R1CH[NH-(SO₂)m-R3]CO-A-B-X [R1 = (SO₂)n-C₁-6alkylene-COOH or an ester derivative thereof; n = 0, 1; m = 0, 1; and m and n are not 1 at the same time; R2 = H, alkyl, alkenyl, cycloalkyl, alklenecycloalkyl, aryl, etc.; R3 = a hydrophobic moiety; or R2 and R3 are a 5- or 6-membered ring together with the N and C to which they are bound, which ring may be fused with an aliphatic or aromatic

6-membered

ring; A = (un)substituted proline optionally containing a second O, N, or S heteroatom, 3,4-dehydroproline, 2-azetidine carboxylic acid, pipecolinic acid, octahydroindole-2-carboxylic acid, 2-aminoisobutyric acid, valine; B = lysine, 4-aminocyclohexylglycine; X = CHF₂, CF₃, COOR₄, CONR₅R₆, 2-thiazole, (un)substituted heterocycle; R₄ = H, alkyl; R₅ and R₆ = independently H, alkyl, alkylene-C₆H₅; R₅ and R₆ together = C₃-6 alkylene] or a pharmaceutically acceptable salt thereof, were prepared as thrombin inhibitors. Thus, HO₂CCH₂-D-(p-methoxy-phenylalanyl)-Pro-Lys-CO₂H was prepared and assayed for anti-thrombin activity (IC₅₀ = 0.044 μM). The compds. of the invention have anticoagulant activity and can be used in treating or preventing thrombin-related diseases.

L99 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:441337 HCAPLUS

DOCUMENT NUMBER: 131:58825

TITLE: Preparation of 8-benzocycloalkyl-1,3,8-triaza[4.5]decan-4-ones as orphanin FQ receptor ligands

INVENTOR(S): Jenck, Francois; Monsma, Frederick; Galley, Guido; Adam, Geo; Cesura, Andrea; Rover, Stephan; Wichmann, Juergen

PATENT ASSIGNEE(S): F.Hoffmann-La Roche Ag, Switz.

SOURCE: Can. Pat. Appl., 45 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2226058	AA	19980730	CA 1997-2226058	19971231
SG 71077	A1	20000321	SG 1998-62	19980107
US 6071925	A	20000606	US 1998-9457	19980120
EP 856514	A1	19980805	EP 1998-100970	19980121
EP 856514	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ES 2158622	T3	20010901	ES 1998-100970	19980121
PT 856514	T	20011031	PT 1998-100970	19980121
ZA 9800570	A	19980730	ZA 1998-570	19980123
CN 1191862	A	19980902	CN 1998-103687	19980123
CN 1113881	B	20030709		
IL 123036	A1	20001206	IL 1998-123036	19980123

NO 9800332	A	19980731	NO 1998-332	19980126
NO 310026	B1	20010507		
JP 10212290	A2	19980811	JP 1998-13711	19980127
JP 3292457	B2	20020617		
HR 980043	B1	20011231	HR 1998-980043	19980127
AU 9852809	A1	19980806	AU 1998-52809	19980129
AU 730147	B2	20010301		
BR 9800524	A	20000314	BR 1998-524	19980130
TW 457238	B	20011001	TW 1998-87101434	19980204
GR 3036523	T3	20011231	GR 2001-401383	20010905
PRIORITY APPLN. INFO.:				
			EP 1997-101409	A 19970130
			EP 1997-119311	A 19971105
			EP 1998-100970	A 19980121

OTHER SOURCE(S): MARPAT 131:58825

ED Entered STN: 19 Jul 1999

AB Title compds. [I; R₁,R₂ = H, halo, alkyl, alkoxy; R₃ = (un)substituted Ph; R₄ = H, alk(en)yl, alkanoyl, Bz, etc.; Z = atoms to complete an (un)substituted 4 to 7-membered ring optionally containing O or S] were prepared

Thus, 6-chloro-2-tetralone was condensed with 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one to give, after reduction, title compound II. Data for biol. activity of I were given.

L99 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:594749 HCAPLUS

DOCUMENT NUMBER: 127:263061

TITLE: Serine protease inhibitors

INVENTOR(S): Adang, Anton Egbert Peter; Peters, Jacobus Albertus Maria

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.; Adang, Anton Egbert Peter; Peters, Jacobus Albertus Maria

SOURCE: PCT Int. Appl., 86 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731939	A1	19970904	WO 1997-EP939	19970226
W: AU, BA, BR, CA, CN, CU, CZ, GH, HU, IL, JP, KR, LC, MX, NO, NZ, PL, RU, SG, TR, US, YU				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IL 120311	A1	20011031	IL 1997-120311	19970225
TW 523513	B	20030311	TW 1997-86102260	19970225
CA 2246722	AA	19970904	CA 1997-2246722	19970226
AU 9717956	A1	19970916	AU 1997-17956	19970226
AU 715765	B2	20000210		
CN 1212705	A	19990331	CN 1997-192688	19970226
BR 9707812	A	19990727	BR 1997-7812	19970226
JP 2000506838	T2	20000606	JP 1997-530601	19970226
EP 1012164	A1	20000628	EP 1997-903384	19970226
EP 1012164	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
RU 2172321	C2	20010820	RU 1998-118048	19970226
AT 277074	E	20041015	AT 1997-903384	19970226
ZA 9701733	A	19970910	ZA 1997-1733	19970227
NO 9803992	A	19981030	NO 1998-3992	19980831

US 6218365	B1	20010417	US 1998-142068	19980831
PRIORITY APPLN. INFO.:			EP 1996-200545	A 19960301
			WO 1997-EP939	W 19970226

OTHER SOURCE(S) : MARPAT 127:263061

ED Entered STN: 17 Sep 1997

AB Peptides A-B-X-NHCH(COR)(CH₂)nC₅H₁₀N (C₅H₁₀N = 4-piperidinyl; A = H, optionally substituted DL- α -hydroxyacetyl, acyl, alkyl, alkylsulfonyl, N-protecting group, etc.; B = bond, amino acid residue; X = amino acid residue; R = H, CHF₂, CF₃, acyl, heterocyclyl; n = 0-3) or their prodrugs or pharmaceutically acceptable salts were prepared as serine protease inhibitors. Thus, HO₂CCH₂-D-Phe-Pro-Ppa Ψ [COCO]-OH [Ppa Ψ [COCO]-OH is NHCH(CO₂H)CH₂C₅H₁₀N] was prepared and assayed for anti-thrombin activity (IC₅₀ = 0.54 μ M).

L99 ANSWER 17 OF 46 HCPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:433709 HCPLUS

DOCUMENT NUMBER: 127:51011

TITLE: Preparation of peptides and thrombin inhibitors

INVENTOR(S): Adang, Anton Egbert Peter; Van Boeckel, Constant
Adriaan Anton; Grootenhuis, Peter Diederik Jan;
Peters, Jacobus Albertus Maria

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9717363	A1	19970515	WO 1996-EP4785	19961030
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, PL, RU, TR, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IL 119466	A1	20010826	IL 1996-119466	19961022
ZA 9608922	A	19970528	ZA 1996-8922	19961023
CA 2235586	AA	19970515	CA 1996-2235586	19961030
AU 9674975	A1	19970529	AU 1996-74975	19961030
AU 712940	B2	19991118		
EP 858464	A1	19980819	EP 1996-937337	19961030
EP 858464	B1	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1202902	A	19981223	CN 1996-198628	19961030
BR 9611377	A	19990223	BR 1996-11377	19961030
JP 11515033	T2	19991221	JP 1996-517828	19961030
RU 2178796	C2	20020127	RU 1998-110641	19961030
AT 239755	E	20030515	AT 1996-937337	19961030
PT 858464	T	20030829	PT 1996-937337	19961030
ES 2199302	T3	20040216	ES 1996-937337	19961030
TW 486459	B	20020511	TW 1996-85113438	19961104
NO 9801965	A	19980630	NO 1998-1965	19980430
US 2001007764	A1	20010712	US 1998-68074	19980503
US 6432921	B2	20020813		
US 2002142967	A1	20021003	US 2002-39737	20020104
PRIORITY APPLN. INFO.:			EP 1995-202982	A 19951103
			EP 1995-203554	A 19951219
			WO 1996-EP4785	W 19961030
			US 1998-68074	A3 19980503

OTHER SOURCE(S) : MARPAT 127:51011

ED Entered STN: 12 Jul 1997
 AB Non-slow-binding thrombin inhibitors of formula A-B-C-Lys-D [A = H, 2-hydroxy-3-cyclohexylpropionyl, R1, R1OCO, R1CO, R1SO₂, (CHR₂)nCOOR₃, or an N-protecting group (R1 = alkylene-COOH, alkyl, alkenyl, aryl, etc.; R2 = H or R1; R3 = H, alkyl, alkenyl, aryl, etc.; n = 1-3); B = bond, L-Asp, Leu, a D-amino acid having a hydrophobic aromatic side chain, etc.; C is an amino acid, e.g., Azt, Pro, and Pec; D = COOH, tetrazole, oxazole, thiazole, benzothiazole] or their prodrugs were prepared. Thus, H-D-Phe-(N-cyclopentyl)-Gly-Lys-(2-thiazolyl) was prepared and assayed for anti-thrombin activity (IC₅₀ = 4.5 μM).

L99 ANSWER 18 OF 46 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2006-133404 [14] WPIX
 DOC. NO. CPI: C2006-046041
 TITLE: New sulfonamide derivatives are gamma-secretase inhibitors useful to treat Alzheimer's disease, breast cancer, cervical cancer and malignancy of the hematopoietic system.
 DERWENT CLASS: B02 B03
 INVENTOR(S): GALLEY, G; JAKOB-ROETNE, R; KITAS, E A
 PATENT ASSIGNEE(S): (GALL-I) GALLEY G; (JAKO-I) JAKOB-ROETNE R; (KITA-I) KITAS E A; (HOFF) HOFFMANN LA ROCHE & CO AG F
 COUNTRY COUNT: 111
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2006014945	A1	20060119 (200614)*		72	
WO 2006005486	A1	20060119 (200614)	EN		
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU LV MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2006014945	A1	US 2005-179703	20050712
WO 2006005486	A1	WO 2005-EP7268	20050706

PRIORITY APPLN. INFO: EP 2004-103339 20040713

ED 20060227

AB US2006014945 A UPAB: 20060227

NOVELTY - Sulfonamide derivatives (I) and their acid addition salts, optically pure enantiomers, racemates or diastereomeric mixtures are new.

DETAILED DESCRIPTION - Sulfonamide derivatives of formula (I) and their acid addition salts, optically pure enantiomers, racemates or diastereomeric mixtures are new.

R1 = (hetero)aryl (optionally substituted with halo, lower alkyl (substituted by halo), -O-lower alkyl (substituted by halo), CF₃, OCF₃, NO₂ or CN);

R2-R4, R-2a, R-3a, R-4a = H, lower alkyl (substituted by halo), CF₃ or phenyl;

R5 = cycloalkyl, (hetero)aryl (both optionally substituted by one or

more substituents of halo, lower alkyl, lower alkoxy, CN, NO₂, amino, OH, lower alkyl (substituted by OH), lower alkyl (substituted by halo), (hetero)aryl (substituted by -C(O)-NR₁₂, -(CR₂)m-C(O)-R-a, -(CH₂)m-heterocycloalkyl), -(CH₂)m-heteroaryl (optionally substituted by -(CH₂)m-lower alkoxy, lower alkyl, -(CH₂)m-O-benzyl or CH₂OH), -O-C(O)-lower alkyl, -C(O)-NR₂, -O-(CH₂)m-C(O)OH, -O-lower alkynyl, -O-lower alkyl (substituted by halo), -O-(CH₂)m-heterocyclyl, -O-(CH₂)m-phenyl (optionally substituted by OH), -O-(CH₂)m-heteroaryl (optionally substituted by lower alkyl, -(CH₂)m-NH-C(O)R-a, -(CH₂)m-NH-S(O)₂-R-a, -S(O)₂-lower alkyl, -S(O)₂-heterocyclyl, -S(O)₂NH-cycloalkyl or cycloalkyl)), CHO, CN, OH, lower alkyloxy, lower alkinyloxy, -OCF₃, OCF₂, OCH₂F, -OC(O)-lower alkyl, -OC(O)-NR-aR-b, -O-(CH₂)n-hetrocyloalkyl, -O-(CH₂)n-hetroaryl (optionally substituted by lower alkyl), -O-(CH₂)n-aryl, -(CH₂)n-C(O)NR-aR-b, -(CH₂)n-C(O)O-lower alkyl, -(CH₂)n-C(O)OH, -(CH₂)n-C(O)O-lower alkynyl, -C(O)-heterocycloalkyl (optionally substituted by COOH), -C(O)-cycloalkyl, -C(O)-aryl, -NR-aR-b, NO₂, -S(O)₂-lower alkyl, -S(O)₂-cyclo alkyl, -S(O)₂-heterocycloalkyl, -S(O)₂-aryl, -S(O)₂-N-aR-b, benzo(1,3)dioxole-5-yl or 2,3-dihydrobenzo(1,4)dioxine-6-yl;

R-a = (hetero)cycloalkyl (optionally substituted by one or more substituents of COOH, -C(O)O-lower alkyl, -CH₂C(O)O-lower alkyl, halo, lower alkyl, phenyl, benzyl, heteroaryl, -(CH₂)m-lower alkoxy or -(CHR)m-C(O)O-lower alkyl), heteroaryl, di-lower alkylamino, CH₂CF₃, -CH₂CHF₂, -CH₂CH₂F, -C(O)-lower alkyl, -C(O)O-lower alkyl, -C(O)-cycloalkyl, H, lower alkyl, lower alkinyloxy or OH;

R-b = H, cycloalkyl (optionally substituted by halo, lower alkyl (substituted by halo), lower alkyl (substituted by OH), -(CH₂)m-heterocycloalkyl, -NR₂, heteroaryl, benzyl or -(CHR)m-C(O)O-lower alkyl), heterocycloalkyl, heteroaryl, di-lower alkylamino, -CH₂CF₃, -CH₂CHF₂, -CH₂CH₂F, -C(O)-lower alkyl, -C(O)O-lower alkyl or C(O)-cycloalkyl;

R, R₆ = H or lower alkyl;

X = -CHR-, a bond, lower alkyl or lower alkenyl; and

m, n = 0-3.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Neuroprotective; Nootropic; Cytostatic.

MECHANISM OF ACTION - Gamma (gamma)-secretase inhibitor. The ability of (I) to inhibit gamma-secretase was tested using biological assays. The results showed that the median inhibitory concentration of rac-4-(((4-chloro-benzenesulfonyl)-(5,5-dimethyl-2-oxazepan-3-yl)-amino)-methyl)-N-methyl-benzamide was 0.01 μM.

USE - (I) are useful for treating Alzheimer's disease, breast cancer, cervical cancer and malignancy of the hematopoietic system (claimed).

Dwg.0/0

L99 ANSWER 19 OF 46 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2005-012791 [01] WPIX
 DOC. NO. CPI: C2005-003465
 TITLE: New 1,4-benzoxazepine-5-carboxamide derivatives are gamma-secretase inhibitors useful to treat Alzheimer's disease.
 DERWENT CLASS: B02
 INVENTOR(S): GALLEY, G; GOODNOW, R A; PETERS, J U;
 GOODNOW, R; PETERS, J
 PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (GALL-I) GALLEY G;
 (GOOD-I) GOODNOW R A; (PETE-I) PETERS J; (HOFF) HOFFMANN LA ROCHE INC
 COUNTRY COUNT: 109
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004100958	A1	20041125 (200501)*	EN	63	
RW:	AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW				
US 2004235819	A1	20041125 (200501)			
AU 2004238037	A1	20041125 (200604)			
EP 1631296	A1	20060308 (200618) EN			
R:	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PL PT RO SE SI SK TR				
US 7060698	B2	20060613 (200639)			
MX 2005012368	A1	20060201 (200643)			
BR 2004010647	A	20060704 (200645)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004100958	A1	WO 2004-EP5177	20040514
US 2004235819	A1	US 2004-838054	20040503
AU 2004238037	A1	AU 2004-238037	20040514
EP 1631296	A1	EP 2004-732944	20040514
US 7060698	B2	WO 2004-EP5177	20040514
MX 2005012368	A1	US 2004-838054	20040503
BR 2004010647	A	WO 2004-EP5177	20040514
		WO 2004-EP5177	20040514
		MX 2005-12368	20051116
		BR 2004-10647	20040514
		WO 2004-EP5177	20040514

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004238037	A1 Based on	WO 2004100958
EP 1631296	A1 Based on	WO 2004100958
MX 2005012368	A1 Based on	WO 2004100958
BR 2004010647	A Based on	WO 2004100958

PRIORITY APPLN. INFO: EP 2003-11040 20030519

ED 20050103

AB WO2004100958 A UPAB: 20050103

NOVELTY - 1,4-benzoxazepine-5-carboxamide derivatives (I) and their acid addition salts are new.

DETAILED DESCRIPTION - 1,4-benzoxazepine-5-carboxamide derivatives of formula (I) and their acid addition salts are new.

R1 = H, lower alkoxy, halo or -NRR';

R, R' = H or lower alkyl;

R2 = H, lower alkyl, -(CH₂)_m-cycloalkyl, -(CH₂)_m-phenyl or -(CH₂)_m-O-lower alkyl;

m = 0-2;

R3 = lower alkyl, -(CH₂)_m-C(O)O-lower alkyl, cycloalkyl or -(CH₂)_m-phenyl (optionally substituted by 1-2 halo or lower alkyl);R4 = -(CH₂)_n-phenyl (optionally substituted by 1-2 of halo, CF₃, -NRR', NO₂ or -SO₂NH₂), cycloalkyl (optionally substituted by phenyl), -(CRR')_n-HET, tetrahydronaphthalen-1-yl, -CHR-naphthalen-2-yl,

fluoren-9-yl, -(CH₂)_o-S-lower alkyl, -(CH₂)_o-S-benzyl, -(CH₂)_o-C(O)NH₂, -(CH₂)_oNRR', -CH(C(O)NH₂)-(CH₂)_o-phenyl, -(CH₂)_o-CF₃ or -(CH₂)_o-CRR'-CH₂-NRR';
 HET = tetrahydropyran-4-yl, pyridin-3-yl, indol-3-yl (all optionally substituted by halo or lower alkoxy), thiophen-2-yl, furan-2-yl, -NH-pyridin-2-yl (all optionally substituted by NO₂), benzimidazol-2-yl, 2-oxo-tetrahydrofuran, 1-benzylpiperidin-4-yl or benzo(1,3)dioxol-5-yl; and
 o, n = 1 or 2.

An INDEPENDENT CLAIM is also included for the preparation of (I).
 ACTIVITY - Neuroprotective; Nootropic.

MECHANISM OF ACTION - gamma -secretase inhibitor. (I) was tested for its gamma -secretase inhibitory activity in Hek293 membrane. The results showed that the median inhibitory concentration of 7-bromo-4-(2,6-difluorobenzyl)-2-isopropyl-3-oxo-2,3,4,5-tetrahydrobenzo(f) (1,4)oxazepine-5-carboxylic acid cyclohexylamide (Ia) was 0.28. The units are not given.

USE - (I) are useful as medicaments in the treatment of Alzheimer's disease (claimed).

Dwg.0/0

L99 ANSWER 20 OF 46 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2002-083069 [11] WPIX
 DOC. NO. CPI: C2002-025204
 TITLE: New 1,4-diazepan-2,5-dione derivatives are neurokinin-1 receptor antagonists, useful for treating e.g. migraine, rheumatoid arthritis, asthma and inflammatory bowel disease.
 DERWENT CLASS: B03
 INVENTOR(S): GALLEY, G; GODEL, T; GOERGLER, A;
 HECK, R; GLLY, G
 PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (GALL-I) GALLEY G;
 (GODE-I) GODEL T; (GOER-I) GOERGLER A; (HECK-I) HECK R;
 (HOFF) HOFFMANN LA ROCHE INC
 COUNTRY COUNT: 92
 PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG
WO 2001090083	A1 20011129 (200211)* EN	38		
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW				
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CO CU CZ DE DK EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW				
US 2002010174	A1 20020124 (200214)			
AU 2001081778	A 20011203 (200221)			
US 6452001	B2 20020917 (200264)			
EP 1296961	A1 20030402 (200325) EN			
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR				
KR 2003003759	A 20030110 (200333)			
BR 2001011062	A 20030610 (200341)			
CN 1430611	A 20030716 (200363)			
JP 2003534332	W 20031118 (200401)	63		
MX 2002011464	A1 20030401 (200415)			
ZA 2002008940	A 20040428 (200432)	24		
AU 2001281778	B2 20050602 (200544)			
MX 230349	B 20050905 (200617)			
CN 1178923	C 20041208 (200618)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001090083	A1	WO 2001-EP5723	20010518
US 2002010174	A1	US 2001-854885	20010514
AU 2001081778	A	AU 2001-81778	20010518
US 6452001	B2	US 2001-854885	20010514
EP 1296961	A1	EP 2001-960225	20010518
		WO 2001-EP5723	20010518
KR 2003003759	A	KR 2002-715837	20021122
BR 2001011062	A	BR 2001-11062	20010518
		WO 2001-EP5723	20010518
CN 1430611	A	CN 2001-809933	20010518
JP 2003534332	W	JP 2001-586272	20010518
		WO 2001-EP5723	20010518
MX 2002011464	A1	WO 2001-EP5723	20010518
		MX 2002-11464	20021121
ZA 2002008940	A	ZA 2002-8940	20021104
AU 2001281778	B2	AU 2001-281778	20010518
MX 230349	B	WO 2001-EP5723	20010518
		MX 2002-11464	20021121
CN 1178923	C	CN 2001-809933	20010518

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001081778	A Based on	WO 2001090083
EP 1296961	A1 Based on	WO 2001090083
BR 2001011062	A Based on	WO 2001090083
JP 2003534332	W Based on	WO 2001090083
MX 2002011464	A1 Based on	WO 2001090083
AU 2001281778	B2 Previous Publ. Based on	AU 2001281778 WO 2001090083
MX 230349	B Based on	WO 2001090083

PRIORITY APPLN. INFO: EP 2000-111249 20000525

ED 20020215

AB WO 200190083 A UPAB: 20021031

NOVELTY - 1,4-Diazepan-2,5-dione derivatives (I), and their addition salts and enantiomeric forms are new.

DETAILED DESCRIPTION - 1,4-Diazepan-2,5-dione derivatives of formula (I), their addition salts and enantiomeric forms are new.

R₁, R₂ = aryl or heteroaryl (containing one or two heteroatoms selected from N, O or S) (both optionally mono, di or tri substituted with T);

T = halo, CF₃, lower alkoxy or lower alkyl;

R₃ = H, lower alkyl, -(CH₂)_nN(R)₂ or -(CH₂)_nheteroaryl or

-(CH₂)_n-non-aromatic heterocycle (heterocycles optionally substituted by T);

R₄ = =O, =N(CH₂)_nCH₃ or =N(CH₂)_nN(R)₂; or

NR₃R₄C = a group of formula -CR₅=N-N=;

R₅ = H, -(CH₂)_nN(R)₂ or -(CH₂)_nheteroaryl or -(CH₂)_n-non-aromatic heterocycle (heterocycles optionally substituted by T);

R = H or lower alkyl; and

n = 0 - 3.

An INDEPENDENT CLAIM is also included for preparations of (I).

ACTIVITY - Antimigraine; antirheumatic; antiarthritic; antiasthmatic;

antiinflammatory; antiparkinsonian; analgesic; nootropic; neuroprotective; antiallergic; antiemetic; antidepressant; tranquilizer; antidote; antiulcer; uropathic; respiratory; ophthalmological; cardiant.

MECHANISM OF ACTION - Neurokinin-1 (NK-1) receptor antagonist.

The affinity of (4S)-4-(3,4-dichloro-benzyl)-6-(2-methoxy-naphthalen-1-yl-methyl)-7,8-dihydro-6H-1,2,3a,6-tetraaza-azulen-5-one (Ia) for the NK1 receptor was evaluated at human NK1 receptor in Chinese hamster ovary cells infected with human NK1 receptor and radiolabelled with (3H) substance P. The affinity to the NK-1 receptor was pKi = 8.76.

USE - For treatment of diseases related to the NK-1 receptor antagonists (claimed) such as migraine, rheumatoid arthritis, asthma, inflammatory bowel disease as well as mediation of the emetic reflex and the modulation of central nervous system (CNS) disorders such as Parkinson's disease and anxiety pain, headache especially migraine, Alzheimer's disease, multiple sclerosis, attenuation of morphine withdrawal, cardiovascular changes, edema, chronic inflammatory diseases and other respiratory diseases including allergic rhinitis, inflammatory diseases of the gut including ulcerative colitis and Crohn's disease, ocular injury and ocular inflammatory diseases, treatment of certain forms of urinary incontinence, for the treatment of a number of physiological disorders associated with an excess or imbalance of tachykinin, anxiety, depression and psychosis. Also in the treatment of motion sickness and vomiting.

ADVANTAGE - The compounds provides adsorption, pharmacokinetics in distribution and transport to the brain. The compounds are useful in treatment of various diseases.

Dwg.0/0

L99 ANSWER 21 OF 46 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 1998-400862 [35] WPIX
 DOC. NO. CPI: C1998-121461
 TITLE: New 1,3,8-triazaspiro-[4.5]-decan-4-one derivatives are Orphanin FQ receptor agonists and antagonists - used to treat e.g. anxiety, stress, depression, trauma, memory loss due to Alzheimer's disease, epilepsy, convulsions, pain and obesity.
 DERWENT CLASS: B02 B03
 INVENTOR(S): ADAM, G; CESURA, A; GALLEY, G; JENCK, F;
 MONSMA, F; ROVER, S; WICHMANN, J; ROEVER, S; WICKMANN, J
 PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) HOFFMANN LA ROCHE F; (HOFF) HOFFMANN LA ROCHE INC
 COUNTRY COUNT: 41
 PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG
<hr/>				
EP 856514	A1 19980805 (199835)* EN 26			
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI				
CZ 9800273	A3 19980812 (199839)			
NO 9800332	A 19980731 (199840)			
JP 10212290	A 19980811 (199842)	20		
AU 9852809	A 19980806 (199843)			
HU 9800138	A2 19980928 (199846)			
ZA 9800570	A 19981028 (199848)	46		
CA 2226058	A 19980730 (199850)			
KR 98070900	A 19981026 (199953)			
SG 71077	A1 20000321 (200022)			
BR 9800524	A 20000314 (200027)			
NZ 329627	A 19991129 (200031)			

US 6071925	A	20000606 (200033)
MX 9800824	A1	19990801 (200063)
IL 123036	A	20001206 (200103)
AU 730147	B	20010301 (200117)
EP 856514	B1	20010613 (200134) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI		
NO 310026	B1	20010507 (200134)
DE 69800896	E	20010719 (200148)
ES 2158622	T3	20010901 (200161)
KR 274107	B	20001215 (200174)
JP 3292457	B2	20020617 (200242) 20
TW 457238	A	20011001 (200243)
CN 1191862	A	19980902 (200276)
MX 205839	B	20020109 (200301)
CN 1113881	C	20030709 (200545)
IN 9800058	I4	20050304 (200555) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 856514	A1	EP 1998-100970	19980121
CZ 9800273	A3	CZ 1998-273	19980129
NO 9800332	A	NO 1998-332	19980126
JP 10212290	A	JP 1998-13711	19980127
AU 9852809	A	AU 1998-52809	19980129
HU 9800138	A2	HU 1998-138	19980126
ZA 9800570	A	ZA 1998-570	19980123
CA 2226058	A	CA 1997-2226058	19971231
KR 98070900	A	KR 1998-2475	19980130
SG 71077	A1	SG 1998-62	19980107
BR 9800524	A	BR 1998-524	19980130
NZ 329627	A	NZ 1998-329627	19980123
US 6071925	A	US 1998-9457	19980120
MX 9800824	A1	MX 1998-824	19980129
IL 123036	A	IL 1998-123036	19980123
AU 730147	B	AU 1998-52809	19980129
EP 856514	B1	EP 1998-100970	19980121
NO 310026	B1	NO 1998-332	19980126
DE 69800896	E	DE 1998-600896	19980121
		EP 1998-100970	19980121
ES 2158622	T3	EP 1998-100970	19980121
KR 274107	B	KR 1998-2475	19980130
JP 3292457	B2	JP 1998-13711	19980127
TW 457238	A	TW 1998-101434	19980204
CN 1191862	A	CN 1998-103687	19980123
MX 205839	B	MX 1998-824	19980129
CN 1113881	C	CN 1998-103687	19980123
IN 9800058	I4	IN 1998-CH58	19980108

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 730147	B Previous Publ.	AU 9852809
NO 310026	B1 Previous Publ.	NO 9800332
DE 69800896	E Based on	EP 856514
ES 2158622	T3 Based on	EP 856514
KR 274107	B Previous Publ.	KR 98070900
JP 3292457	B2 Previous Publ.	JP 10212290

PRIORITY APPLN. INFO: EP 1997-119311 19971105; EP
1997-101409 19970130

ED 19980904

AB EP 856514 A UPAB: 19981021

1,3,8-Triazaspiro[4.5]-decan-4-one derivatives of formula (I) and their acid addition salts are new. R₁, R₂ = H, lower alkyl, lower alkoxy or halo; R₃ = phenyl (optionally substituted by lower alkyl, CF₃, lower alkoxy or halo); R₄ = H, lower alkyl, lower alkenyl, C(O)-lower alkyl, C(O)-phenyl, lower alkyl-C(O)-phenyl, lower alkynene-C(O)-lower alkyl, lower alkantriyl-di-C(O)-lower alkyl, hydroxy lower alkyl, lower alkyl-O-lower alkyl, lower alkyl-CH(OH)CF₃, phenyl or benzyl; R₅, R₆ = H, phenyl, lower alkyl, di-lower alkyl; or R₅+R₆ = phenyl; or R₅+R₁ or R₅+R₂ = optionally saturated 6-membered ring; and A = 4-7-membered saturated ring optionally containing a heteroatom e.g. O or S.

USE - (I) are Orphanin FQ (OFQ) receptor antagonists and agonists and are used in the treatment of OFQ receptor-related diseases including psychiatric, neurological and physiological disorders (e.g. anxiety and stress disorders, depression, trauma, memory loss due to Alzheimer's disease or other dementias, epilepsy and convulsions, acute and/or chronic pain conditions, symptoms of withdrawal from addictive drugs, control of water balance, sodium ion excretion, arterial blood pressure disorders and eating disorders such as obesity) (all claimed). (I) are administered orally, rectally or parenterally at a daily dosage of 10-1000 mg.

Dwg.0/0

L99 ANSWER 22 OF 46 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1992-270475 [33] WPIX

DOC. NO. CPI: C1992-120581

TITLE: Modified partial sequences of human fibrinogen inhibit factor IIA - for use as anticoagulants in treating pulmonary embolism, thrombo phlebitis etc..

DERWENT CLASS: B04 B05

INVENTOR(S): JETTEN, W; OTTENHEYM, H C J; PETERS, J A M;
VAN, NISPEN J W F M; VISSER, A; VAN, NISPEN J W; VAN,
NISPEN J W F

PATENT ASSIGNEE(S): (ALKU) AKZO NV; (ALKU) AKZO NOBEL NV

COUNTRY COUNT: 23

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG
EP 498508	A1 19920812 (199233)*	EN	18	
R: PT				
WO 9213877	A1 19920820 (199236)		30	
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE				
W: AU CA FI JP KR NO US				
AU 9211933	A 19920907 (199249)			
FI 9303454	A 19930803 (199343)			
NO 9302769	A 19930803 (199344)			
EP 570428	A1 19931124 (199347)	EN		
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE				
JP 06505001	W 19940609 (199427)		20	
AU 656947	B 19950223 (199515)			
US 5719128	A 19980217 (199814)		15	
EP 570428	B1 19981216 (199903)	EN		
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE				
DE 69227895	E 19990128 (199910)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 498508	A1	EP 1992-200312	19920204
WO 9213877	A1	WO 1992-EP273	19920204
AU 9211933	A	AU 1992-11933	19920204
		WO 1992-EP273	19920204
FI 9303454	A	WO 1992-EP273	19920204
		FI 1993-3454	19930803
NO 9302769	A	WO 1992-EP273	19920204
		NO 1993-2769	19930803
EP 570428	A1	EP 1992-903870	19920204
		WO 1992-EP273	19920204
JP 06505001	W	JP 1992-503954	19920204
		WO 1992-EP273	19920204
AU 656947	B	AU 1992-11933	19920204
US 5719128	A	WO 1992-EP273	19920204
	Cont of	US 1993-98281	19930916
		US 1995-458997	19950602
EP 570428	B1	EP 1992-903870	19920204
		WO 1992-EP273	19920204
DE 69227895	E	DE 1992-627895	19920204
		EP 1992-903870	19920204
		WO 1992-EP273	19920204

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9211933	A Based on	WO 9213877
EP 570428	A1 Based on	WO 9213877
JP 06505001	W Based on	WO 9213877
AU 656947	B Previous Publ.	AU 9211933
	Based on	WO 9213877
US 5719128	A Based on	WO 9213877
EP 570428	B1 Based on	WO 9213877
DE 69227895	E Based on	EP 570428
	Based on	WO 9213877

PRIORITY APPLN. INFO: EP 1991-200201 19910204

ED 19930806

AB EP 498508 A UPAB: 19950306

Peptides of formula X-Y-Z-A-P-Q-T (I) and their pharmaceutically acceptable salts are new. X1 if present, = H, Me acyl, a protecting gp., or is connected to T; Y = Phe, DPA (diphenylalanyl), Val, Ile or Nle (all D-form) or a gp. (II)-(IV) R6 = H, alkyl, N-alkyl or N-dialkyl; Z, if present is Gly, opt. substd. L/D-Pro homologue, L/D-Ala, L/D-Val, L/D-Leu, Aib (aminoisobutyric acid) or L/D-Pro; A = (Nn)e CR1R7-M-CR2R8 (CH₂)_q-CO-; M = (CO)dNH, (CO)d(CH₂)p, CONMe, CHOH-(CH₂)-p or CO-CF₂(-CO)-s; d = 0-2; p and q = 0-5; e and s = 0 or 1; R1 = side chain of a hydrophobic, basic amino acid, aliphatic or aromatic; R2 = H, Me, CH₂OH or benzyl; R7 and R8 are each H, Me or 1-3C alkyl; alternatively, A is (V) W is CH₂, CO(CH₂)_q, CHOH-(CH₂)-q or CO-CF₂(-CO)-s; i = 1 or 2; R3 = H, Me or COOH attached to ring CH₂; Q (when present) and P = Phe, Cha (cyclohexylalanyl), Nal (1 or 2) (naphthylalanyl), phenylglycyl, Leu, Ile, Nle, Arg, Lys or His (all L/D) or Har (homoarginine), Hly (homolysine), Pec (pipecolic acid), or D-DPA; or an L/D residue -NH/CHR1-CO-; T = OH, OR₄, NH₂, NHR₄, N(CH₂)₁₋₆NR₄R₅ (Sic), or NR₄R₅; R₄ and R₅ = H, alkyl, aryl or aralkyl, or are bonded together to form a ring; alternatively, T is connected to X.

USE/ADVANTAGE - (I) are powerful and very selective inhibitors of

factor IIa so inhibit production of thrombin and are useful as anticoagulants in human or veterinary medicine, e.g., to prevent or control pulmonary embolism; thrombophlebitis; arterial occlusion; venous or arterial thrombosis, etc. (I) are formulated conventionally for admin. at 0.01-10mg/kg, opt. together with other active cpds. used in acute anticoagulation therapy. They can also be incorporated into slow release implants.

0/0

Dwg.0/0

Dwg.0/0

L99 ANSWER 23 OF 46 MEDLINE on STN DUPLICATE 9
 ACCESSION NUMBER: 2000274975 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10817274
 TITLE: Sedation for pediatric endoscopic procedures.
 AUTHOR: Tolia V; Peters J M; Gilger M A
 CORPORATE SOURCE: Division of Pediatric Gastroenterology and Nutrition, Wayne State University, Children's Hospital of Michigan, Detroit 48201, USA.
 SOURCE: Journal of pediatric gastroenterology and nutrition, (2000 May) Vol. 30, No. 5, pp. 477-85. Ref: 69
 Journal code: 8211545. ISSN: 0277-2116.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200007
 ENTRY DATE: Entered STN: 11 Aug 2000
 Last Updated on STN: 24 Apr 2002
 Entered Medline: 31 Jul 2000
 ED Entered STN: 11 Aug 2000
 Last Updated on STN: 24 Apr 2002
 Entered Medline: 31 Jul 2000

L99 ANSWER 24 OF 46 MEDLINE on STN DUPLICATE 13
 ACCESSION NUMBER: 91153124 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 1963400
 TITLE: Steroid modulation of the GABA_A receptor complex: electrophysiological studies.
 AUTHOR: Lambert J J; Peters J A; Sturgess N C; Hales T G
 CORPORATE SOURCE: Department of Pharmacology & Clinical Pharmacology, Ninewells Hospital & Medical School, Dundee University, UK.
 SOURCE: Ciba Foundation symposium, (1990) Vol. 153, pp. 56-71; discussion 71-82.
 Journal code: 0356636. ISSN: 0300-5208.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199104
 ENTRY DATE: Entered STN: 28 Apr 1991
 Last Updated on STN: 28 Apr 1991
 Entered Medline: 9 Apr 1991
 ED Entered STN: 28 Apr 1991
 Last Updated on STN: 28 Apr 1991
 Entered Medline: 9 Apr 1991
 AB The effect of some endogenous and synthetic steroids on the operation of inhibitory and excitatory amino acid neurotransmitter receptors was examined. Anaesthetic pregnane steroids (e.g. alphaxalone, 5

alpha-pregnan-3 alpha-ol-20-one, 5 alpha-pregnane-3 alpha,21-diol-20-one) potentiated GABAA receptor-mediated whole-cell currents recorded from bovine chromaffin cells. The threshold concentration for enhancement was 10-30 nM. Potentiation was stereoselective and was mediated by a steroid-induced prolongation of the burst duration of the GABA-activated channel. Additionally, the pregnane steroids directly activated the GABAA receptor. Both the potentiation and activation appear to be mediated through a site(s) distinct from the well-known barbiturate and benzodiazepine allosteric sites of the GABAA receptor. Intracellularly applied alphaxalone and 5 beta-pregnan-3 alpha-ol-20-one had no discernible effects on the GABAA receptor, suggesting that the steroid binding site can only be accessed extracellularly. Unlike behaviourally depressant barbiturates, which modulate GABAA receptor function in a manner similar to that of the pregnane steroids, alphaxalone and 5 beta-pregnan-3 alpha-ol-20-one show striking pharmacological selectivity. Voltage-clamp recordings from rat central neurons in culture indicate that pentobarbitone exerts its potentiating and GABA-mimetic effects over a range of concentrations which also depress currents mediated by glutamate receptor subtypes. In contrast, alphaxalone and several endogenous steroids greatly enhance responses to GABA, but have no direct effect on glutamate receptors. Such pharmacological selectivity, coupled with appropriate stereoselectivity of action, suggests that the GABAA receptor mediates some of the behavioural effects of synthetic and endogenous pregnane steroids.

L99 ANSWER 25 OF 46 MEDLINE on STN DUPLICATE 14
 ACCESSION NUMBER: 87186041 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 3032320
 TITLE: Modulation of GABAA receptor activity by alphaxalone.
 AUTHOR: Cottrell G A; Lambert J J; Peters J A
 SOURCE: British journal of pharmacology, (1987 Mar) Vol. 90, No. 3, pp. 491-500.
 Journal code: 7502536. ISSN: 0007-1188.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198705
 ENTRY DATE: Entered STN: 3 Mar 1990
 Last Updated on STN: 3 Mar 1990
 Entered Medline: 28 May 1987
 ED Entered STN: 3 Mar 1990
 Last Updated on STN: 3 Mar 1990
 Entered Medline: 28 May 1987
 AB The modulation of the gamma-aminobutyric acidA (GABAA) receptor by alphaxalone has been investigated by use of voltage-clamp recordings from enzymatically isolated bovine chromaffin cells maintained in cell culture. Alphaxalone (greater than 30 nM) reversibly and dose-dependently potentiated the amplitude of membrane currents elicited by locally applied GABA (100 microm). The potentiation was not associated with a change in the reversal potential of GABA-evoked currents and was not influenced by the benzodiazepine receptor antagonist, Ro15-1788 (300 nM). At relatively high concentrations (greater than 1 microM), alphaxalone directly elicited a membrane current. It is concluded that such currents result from GABAA receptor activation since they were reversibly suppressed by bicuculline (3 microM), dose-dependently enhanced by phenobarbitone (100-500 microm), and had a similar reversal potential (approximately 0 mV) to currents elicited by GABA. Additionally, on outside-out membrane patches, alphaxalone activated single channel currents with amplitudes and a reversal potential similar to those evoked

by GABA. Alphaxalone (30 nM-1 microM) had no effect upon the amplitude of membrane currents elicited by locally applied acetylcholine (ACh) (100 microM). However, higher concentrations of alphaxalone (10-100 microM) reversibly suppressed ACh-evoked currents, the IC₅₀ for blockade being 20 microM. The beta-hydroxy isomer of alphaxalone, betaxalone (100 nM-1 microM), did not potentiate GABA-induced currents, nor did higher concentrations of the steroid (10-100 microM) directly evoke a membrane current. However, over the latter concentration range, betaxalone suppressed the amplitude of currents elicited either by GABA or ACh. The relevance of the present results to the anaesthetic action of alphaxalone is discussed together with the broader implications of steroid modulation of the GABAA receptor.

L99 ANSWER 26 OF 46 MEDLINE on STN DUPLICATE 15
 ACCESSION NUMBER: 87317726 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 2888123
 TITLE: Modulation of the GABAA receptor by progesterone metabolites.
 AUTHOR: Callaghan H; Cottrell G A; Hather N Y; Lambert J J; Nooney J M; Peters J A
 SOURCE: Proceedings of the Royal Society of London. Series B, Containing papers of a Biological character. Royal Society (Great Britain), (1987 Aug 21). Vol. 231, No. 1264, pp. 359-69.
 Journal code: 7505889. ISSN: 0080-4649.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198710
 ENTRY DATE: Entered STN: 5 Mar 1990
 Last Updated on STN: 3 Feb 1997
 Entered Medline: 20 Oct 1987
 ED Entered STN: 5 Mar 1990
 Last Updated on STN: 3 Feb 1997
 Entered Medline: 20 Oct 1987
 AB The naturally occurring progesterone metabolites 5 beta-pregnan-3 alpha-ol-20-one and 5 beta-pregnane-3,20-dione reversibly enhance membrane currents elicited by locally applied GABA in bovine adrenomedullary chromaffin cells. Such potentiation was not influenced by the benzodiazepine antagonist Ro 15-1788. At concentrations in excess of those necessary to evoke potentiation of GABA currents, 5 beta-pregnan-3 alpha-ol-20-one and 5 beta-pregnane-3,20-dione directly activated a membrane conductance. The resulting currents were potentiated by phenobarbitone and diazepam, and abolished by the GABAA-receptor antagonist, bicuculline. On outside-out membrane patches, 5 beta-pregnan-3 alpha-ol-20-one and 5 beta-pregnane-3,20-dione activated single channel currents of similar amplitude to those evoked by GABA. The results suggest that certain naturally occurring steroids potentiate the actions of GABA and, additionally, directly activate the GABAA receptor.

L99 ANSWER 27 OF 46 MEDLINE on STN
 ACCESSION NUMBER: 2004088712 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14660631
 TITLE: The role of phosphorylation in D1 dopamine receptor desensitization: evidence for a novel mechanism of arrestin association.
 AUTHOR: Kim Ok-Jin; Gardner Benjamin R; Williams Daniel B; Marinec Paul S; Cabrera David M; Peters Jennifer D; Mak Chun C; Kim Kyeong-Man; Sibley David R

CORPORATE SOURCE: Molecular Neuropharmacology Section, NINDS, National Institutes of Health, Bethesda, Maryland 20892-1406, USA.

SOURCE: The Journal of biological chemistry, (2004 Feb 27) Vol. 279, No. 9, pp. 7999-8010. Electronic Publication: 2003-12-04. Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200405

ENTRY DATE: Entered STN: 24 Feb 2004
Last Updated on STN: 5 May 2004
Entered Medline: 3 May 2004

ED Entered STN: 24 Feb 2004
Last Updated on STN: 5 May 2004
Entered Medline: 3 May 2004

AB Homologous desensitization of D(1) dopamine receptors is thought to occur through their phosphorylation leading to arrestin association which interdicts G protein coupling. In order to identify the relevant domains of receptor phosphorylation, and to determine how this leads to arrestin association, we created a series of mutated D(1) receptor constructs. In one mutant, all of the serine/threonine residues within the 3rd cytoplasmic domain were altered (3rdTOT). A second construct was created in which only three of these serines (serines 256, 258, and 259) were mutated (3rd234). We also created four truncation mutants of the carboxyl terminus (T347, T369, T394, and T404). All of these constructs were comparable with the wild-type receptor with respect to expression and adenylyl cyclase activation. In contrast, both of the 3rd loop mutants exhibited attenuated agonist-induced receptor phosphorylation that was correlated with an impaired desensitization response. Sequential truncation of the carboxyl terminus of the receptor resulted in a sequential loss of agonist-induced phosphorylation. No phosphorylation was observed with the most severely truncated T347 mutant. Surprisingly, all of the truncated receptors exhibited normal desensitization. The ability of the receptor constructs to promote arrestin association was evaluated using arrestin-green fluorescent protein translocation assays and confocal fluorescence microscopy. The 3rd234 mutant receptor was impaired in its ability to induce arrestin translocation, whereas the T347 mutant was comparable with wild type. Our data suggest a model in which arrestin directly associates with the activated 3rd cytoplasmic domain in an agonist-dependent fashion; however, under basal conditions, this is sterically prevented by the carboxyl terminus of the receptor. Receptor activation promotes the sequential phosphorylation of residues, first within the carboxyl terminus and then the 3rd cytoplasmic loop, thereby dissociating these domains and allowing arrestin to bind to the activated 3rd loop. Thus, the role of receptor phosphorylation is to allow access of arrestin to its receptor binding domain rather than to create an arrestin binding site per se.

L99 ANSWER 28 OF 46 MEDLINE on STN

ACCESSION NUMBER: 85094112 MEDLINE

DOCUMENT NUMBER: PubMed ID: 3966405

TITLE: Effect of the calcium antagonist diltiazem on atrioventricular conduction in chronic atrial fibrillation.

AUTHOR: Theisen K; Haufe M; Peters J; Theisen F;
Jahrmarker H

SOURCE: The American journal of cardiology, (1985 Jan 1) Vol. 55, No. 1, pp. 98-102.
Journal code: 0207277. ISSN: 0002-9149.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198501
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 29 Jan 1985

ED Entered STN: 20 Mar 1990
 Last Updated on STN: 20 Mar 1990
 Entered Medline: 29 Jan 1985

AB The effect of oral diltiazem treatment on the mean ventricular rate was studied in 10 patients with stable atrial fibrillation (AF). The profile of mean ventricular rate was analyzed by means of 24-hour electrocardiographic recordings. Both single-dose (120 mg) and maintenance therapy (80 mg 3 times daily) reduced the mean ventricular rate significantly. After the single dose, the effect set in after 120 +/- 40 minutes (mean +/- standard deviation) and persisted for 347 +/- 84 minutes. Histograms of RR intervals were plotted and their changes after diltiazem therapy were also analyzed. The shortest and longest atrioventricular (AV) conduction times were defined as 5% and 95% values of the cumulative frequency curve, respectively. There were 2 distinct types of the RR-interval histographic changes: In 50% of the patients, the longest and shortest RR intervals prolonged proportionately; in the other 50%, the longest intervals increased disproportionately. Results indicate that oral diltiazem treatment can significantly decrease the mean ventricular rate in patients with AF by influencing the concealed conduction in the AV node. The changes of the RR-interval histograms suggest that in 50% of the patients, the increase of the concealed conduction was probably caused primarily by the increase of AF rate, and in 50% both increased AF rate and prolonged refractory period in the AV node contributed to the increase of concealed conduction.

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ACCESSION NUMBER: 2002008475 EMBASE
TITLE: Modulation of native and recombinant GABA(A) receptors by endogenous and synthetic neuroactive steroids.
AUTHOR: Lambert J.J.; Belelli D.; Harney S.C.; Peters J.A.; Frenguelli B.G.
CORPORATE SOURCE: J.J. Lambert, Neurosciences Institute, University of Dundee, Ninewells Hospital/Medical School, Dundee DD1 9SY, United Kingdom. j.j.lambert@dundee.ac.uk
SOURCE: Brain Research Reviews, (2001) Vol. 37, No. 1-3, pp. 68-80.

Refs: 98
ISSN: 0165-0173 CODEN: BRERD2
S 0165-0173(01)00124-2
PUBLISHER IDENT.:
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
050 Epilepsy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002
ED Entered STN: 17 Jan 2002
Last Updated on STN: 17 Jan 2002

AB Upon administration, certain pregnane steroids produce clear behavioural effects including, anxiolysis, sedation, analgesia, anaesthesia and are anti-convulsant. This behavioural profile is characteristic of compounds that act to enhance the actions of GABA acting at the GABA(A) receptor. In agreement, numerous studies have now demonstrated these steroids to be potent, positive allosteric modulators of the GABA(A) receptor. The pregnane steroids are synthesized in the periphery by endocrine glands such as the adrenals and the ovaries, but are also made by neurons and glial cells in the central nervous system itself. Hence, these compounds could play both an endocrine and a paracrine role to influence neuronal excitability by promoting inhibition. Here we review evidence that the pregnane steroids are highly selective and extremely potent GABA(A) receptor modulators and that their effects at 'physiological' concentrations (low nanomolar) may be influenced by the subunit composition of the GABA(A) receptor. This feature may underlie recent findings demonstrating the effects of the neurosteroids on inhibitory synaptic transmission to be brain region dependent, although recent reports suggest that phosphorylation mechanisms may additionally influence neurosteroid sensitivity of the GABA(A) receptor. Numerous synthetic steroids have been synthesized in an attempt to therapeutically exploit the behavioural effects of the pregnane steroids and progress with this approach will be discussed. However, the demonstration that the steroids may be made within the central nervous system offers the alternative strategy of targeting the enzymes that synthesize/metabolise the neurosteroids to exploit this novel endocrine/paracrine interaction.

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L99 ANSWER 30 OF 46 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 11

ACCESSION NUMBER: 94371220 EMBASE

DOCUMENT NUMBER: 1994371220

TITLE: CSF levels of diazepam-binding inhibitor correlate with REM latency in schizophrenia, a pilot study.

AUTHOR: Van Kammen D.P.; Guidotti A.; Neylan T.; Guarneri P.; Kelley M.E.; Gurkis J.; Gilbertson M.W.; Peters J.L.; Costa E.

CORPORATE SOURCE: Veterans Affairs Medical Center, Pittsburgh, PA 15206, United States

SOURCE: European Archives of Psychiatry and Clinical Neuroscience, (1994) Vol. 244, No. 4, pp. 216-222. .

ISSN: 0940-1334 CODEN: EAPNES

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 29 Dec 1994
Last Updated on STN: 29 Dec 1994

ED Entered STN: 29 Dec 1994
Last Updated on STN: 29 Dec 1994

AB CSF diazepam-binding inhibitor-like immunoreactivity (DBI-LI) and polysomnography were studied in 28 drug-free male schizophrenic (DSM-III-R) patients. They underwent a three-night polysomnography evaluation and a lumbar puncture. CSF DBI-LI correlated positively with REM latency, the REM latency/2(d) nonREM period ratio and stage-4% sleep, and negatively with stage-1% sleep. CSF DBI-LI did not correlate significantly with duration of sleep or sleep latency. CSF DBI-LI during haloperidol treatment did not correlate significantly with sleep EEG

measures. The results of this first study of the relationship between endogenous DBI and sleep in humans suggest that physiological effects of DBI other than interactions with the BZD/GABAA receptor complex may explain its positive effects on sleep. However, the absence of similar sleep data in normal subjects precludes us from establishing a specific relationship between DBI and sleep in schizophrenia.

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ACCESSION NUMBER: 2004394005 EMBASE

TITLE: Fatal propofol infusion syndrome in association with ketogenic diet.

AUTHOR: Baumeister F.A.M.; Oberhoffer R.; Liebhaber G.M.; Kunkel J.; Eberhardt J.; Holthausen H.; Peters J.

CORPORATE SOURCE: Dr. F.A.M. Baumeister, Kinderklinik und Poliklinik, Technischen Universitat Munchen, Kinderklinik Schwabing, Kolner Platz 1, 80804 Munchen, Germany.

FAM.Baumeister@lrz.uni-muenchen.de

SOURCE: Neuropediatrics, (2004) Vol. 35, No. 4, pp. 250-252. .
Refs: 11

ISSN: 0174-304X CODEN: NRPDBB

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 007 Pediatrics and Pediatric Surgery

008 Neurology and Neurosurgery

037 Drug Literature Index

038 Adverse Reactions Titles

050 Epilepsy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 30 Sep 2004

Last Updated on STN: 30 Sep 2004

ED Entered STN: 30 Sep 2004

Last Updated on STN: 30 Sep 2004

AB Propofol is used for the treatment of refractory status epilepticus. When given as a long-term infusion propofol may cause a rare but frequently fatal complication, the propofol infusion syndrome. The hallmarks are metabolic acidosis, lipemia, rhabdomyolysis and myocardial failure. Propofol infusion syndrome is caused by impaired fatty acid oxidation. Beside anticonvulsants the ketogenic diet, a high-fat, low-carbohydrate, adequate-protein diet, is an effective treatment for difficult-to-control seizures. We report a 10-year-old boy with catastrophic epilepsy, who developed fatal propofol infusion syndrome when a ketogenic diet was initiated. Substances like propofol which impair fatty acid oxidation may pose an increased risk if combined with ketogenic diet.

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ACCESSION NUMBER: 2003205705 EMBASE

TITLE: Opioid "holiday" following antagonist supported detoxification during general anesthesia improves opioid agonist response in a cancer patient with opioid addiction.

AUTHOR: Breitfeld C.; Eikermann M.; Kienbaum P.; Peters J.

CORPORATE SOURCE: Dr. C. Breitfeld, Klin. fur Anasthiol./Intensivmedizin, Universitätsklinikum Essen, Hufelandstr. 55, D-45122 Essen, Germany. christa.breitfeld@uni-essen.de

SOURCE: Anesthesiology, (1 Feb 2003) Vol. 98, No. 2, pp. 571-573. .
Refs: 21

ISSN: 0003-3022 CODEN: ANESAV

COUNTRY: United States

DOCUMENT TYPE: Journal; Article
 FILE SEGMENT:
 016 Cancer
 024 Anesthesiology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 040 Drug Dependence, Alcohol Abuse and Alcoholism
 LANGUAGE: English
 ENTRY DATE: Entered STN: 5 Jun 2003
 Last Updated on STN: 5 Jun 2003
 ED Entered STN: 5 Jun 2003
 Last Updated on STN: 5 Jun 2003

L99 ANSWER 33 OF 46 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003455934 EMBASE
 TITLE: Neurosteroid modulation of GABA(A) receptors.
 AUTHOR: Lambert J.J.; Belelli D.; Peden D.R.; Vardy A.W.; Peters J.A.
 CORPORATE SOURCE: J.J. Lambert, Dept. of Pharmacol. and Neuroscience,
 Ninewells Hosp. and Medical School, Dundee University,
 Dundee DD1 9SY, United Kingdom. j.j.lambert@dundee.ac.uk
 SOURCE: Progress in Neurobiology, (2003) Vol. 71, No. 1, pp. 67-80.
 Refs: 108
 ISSN: 0301-0082 CODEN: PGNBAS

COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT:
 008 Neurology and Neurosurgery
 029 Clinical Biochemistry
 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 1 Dec 2003
 Last Updated on STN: 1 Dec 2003
 ED Entered STN: 1 Dec 2003
 Last Updated on STN: 1 Dec 2003
 AB Certain metabolites of progesterone and deoxycorticosterone are established as potent and selective positive allosteric modulators of the γ -aminobutyric acid type A (GABA(A)) receptor. Upon administration these steroids exhibit clear behavioural effects that include anxiolysis, sedation and analgesia, they are anticonvulsant and at high doses induce a state of general anaesthesia, a profile consistent with an action to enhance neuronal inhibition. Physiologically, peripherally synthesised pregnane steroids derived from endocrine glands such as the adrenals and ovaries function as hormones by crossing the blood brain barrier to influence neuronal signalling. However, the demonstration that certain neurons and glial cells within the central nervous system (CNS) can synthesize these steroids either de novo, or from peripherally derived progesterone, has led to the proposal that these steroids (neurosteroids) can additionally function in a paracrine manner, to locally influence GABAergic transmission. Steroid levels are known to change dynamically, for example in stress and during pregnancy. Given that GABA (A) receptors are ubiquitously expressed throughout the central nervous system, such changes in steroid levels would be predicted to cause a global enhancement of inhibitory neurotransmission throughout the brain, a scenario that would seem incompatible with a physiological role as a selective neuromodulator. Here, we will review emerging evidence that the GABA-modulatory actions of the pregnane steroids are highly selective, with their actions being brain region and indeed neuron dependent.

Furthermore, the sensitivity of GABA(A) receptors is not static but can dynamically change. The molecular mechanisms underpinning this neuronal specificity will be discussed with particular emphasis being given to the role of GABA(A) receptor isoforms, protein phosphorylation and local steroid metabolism and synthesis. COPYRIGHT. 2003 Elsevier Ltd. All rights reserved.

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ACCESSION NUMBER: 2003050779 EMBASE
 TITLE: Exploring **benzodiazepine** use among Houston arrestees.
 AUTHOR: Yacoubian Jr. G.S.; Urbach B.J.; Larsen K.L.; Johnson R.J.; Peters Jr. R.J.
 CORPORATE SOURCE: G.S. Yacoubian Jr., McFarland and Associates Inc., 8601 Georgia Avenue, Silver Spring, MD 20910, United States
 SOURCE: Journal of Psychoactive Drugs, (2002) Vol. 34, No. 4, pp. 393-399.
 Refs: 32
 ISSN: 0279-1072 CODEN: JPDRD3
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 037 Drug Literature Index
 040 Drug Dependence, Alcohol Abuse and Alcoholism
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20 Feb 2004
 Last Updated on STN: 20 Feb 2004
 ED Entered STN: 20 Feb 2004
 Last Updated on STN: 20 Feb 2004
 AB While marijuana and cocaine are the two most prevalent drugs among arrestees, **benzodiazepine** use has surpassed that of opiates in several jurisdictions across the United States. Despite this proliferation, few scholarly works have focused on **benzodiazepine** use among individuals under criminal justice supervision. In the present study, the authors used Chi-square statistics and logistic regression to identify significant associations between recent **benzodiazepine** use (as measured by urinalysis), demographic characteristics, and alcohol and other drug (AOD) use among a sample of 1,572 adult Houston arrestees surveyed through the Arrestee Drug Abuse Monitoring (ADAM) Program in 1999. Compared to nonusers, **benzodiazepine**-positive arrestees were more likely to be Black, less likely to have a high school diploma, and more likely to be arrested for a drug- or alcohol-related offense. Moreover, analyses indicated that recent barbiturate, heroin, PCP, and marijuana use, as measured by urinalysis, were the strongest predictors of recent **benzodiazepine** use. Policy implications are assessed in light of the current findings.

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ACCESSION NUMBER: 2002284481 EMBASE
 TITLE: Comparing drug use between welfare-receiving arrestees and non-welfare-receiving arrestees.
 AUTHOR: Yacoubian Jr. G.S.; Peters Jr. R.J.; Urbach B.J.; Johnson R.J.
 CORPORATE SOURCE: G.S. Yacoubian Jr., 4321 Hartwick Rd., College Park, MD 20740, United States
 SOURCE: Journal of Drug Education, (2002) Vol. 32, No. 2, pp. 139-147.
 Refs: 22

ISSN: 0047-2379 CODEN: JDGEBT
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 040 Drug Dependence, Alcohol Abuse and Alcoholism
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 29 Aug 2002
 Last Updated on STN: 29 Aug 2002
 ED Entered STN: 29 Aug 2002
 Last Updated on STN: 29 Aug 2002
 AB The Personal Responsibility and Work Opportunity Reconciliation Act of 1996 (PRWORA) symbolized a comprehensive change to the nation's welfare system. Despite several provisions within PRWORA that focus on the use of illegal drugs, few studies have attempted to identify the prevalence of illegal drug use among welfare recipients. Moreover, no scholarly works have compared rates of drug use in welfare-receiving populations to those of non-welfare-receiving populations with an objective measure of drug use. In the current study, urine specimens were collected from 1,572 arrestees interviewed through Houston's Arrestee Drug Abuse Monitoring (ADAM) Program in 1999. Drug positive rates are compared between welfare-receiving arrestees (n = 116), non-welfare receiving arrestees living below the poverty level (n = 539), and non-welfare receiving arrestees living above the poverty level (n = 917). Welfare-receiving arrestees were more likely to be female, older, less educated, and to test positive for opiates and benzodiazepines than the other subgroups. Implications for welfare reform policy are discussed in light of the current findings.

L99 ANSWER 36 OF 46 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
 ACCESSION NUMBER: 2001292160 EMBASE
 TITLE: Population study of benign rolandic epilepsy: Is treatment needed?.
 AUTHOR: Peters J.M.; Camfield C.S.; Camfield P.R.
 CORPORATE SOURCE: Dr. C.S. Camfield, IWK Health Centre, PO Box 3070, Halifax, NS B3J 3G9, Canada
 SOURCE: Neurology, (14 Aug 2001) Vol. 57, No. 3, pp. 537-539. .
 Refs: 10
 ISSN: 0028-3878 CODEN: NEURAI
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy
 007 Pediatrics and Pediatric Surgery
 008 Neurology and Neurosurgery
 037 Drug Literature Index
 050 Epilepsy
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 6 Sep 2001
 Last Updated on STN: 6 Sep 2001
 ED Entered STN: 6 Sep 2001
 Last Updated on STN: 6 Sep 2001
 AB Forty-three of 79 children (54%) with benign rolandic epilepsy from a regional population were treated with antiepileptic drugs (AED); 36 (46%) were not. Physician advice was a major determinant of treatment choice. AED significantly reduced generalized seizures ($p = 0.001$) but did not reduce partial seizures. After 4 to 14 years and >900 seizures, all patients were in remission without medication or injury. Physicians may confidently offer a no-AED treatment strategy.

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ACCESSION NUMBER: 1999195698 EMBASE
 TITLE: [Opioid detoxification under general anaesthesia - New scientific territory or established routine?]. OPIOID DETOXIFIKATION UNTER ANASTHESIE: WISSENSCHAFTLICHES NEULAND ODER ETABLIERTE METHODE?.
 AUTHOR: Peters J.; Kienbaum P.
 CORPORATE SOURCE: Dr. J. Peters, Abt. Anasthesiologie/Intensivmedizin, Universitätsklinikum GH Essen, Hufelandstrasse 55, D-45122 Essen, Germany
 SOURCE: Anasthesiologie Intensivmedizin Notfallmedizin Schmerztherapie, (1999) Vol. 34, No. 5, pp. 259-260.
 Refs: 9
 ISSN: 0939-2661 CODEN: AISTE5
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; Editorial
 FILE SEGMENT: 024 Anesthesiology
 032 Psychiatry
 037 Drug Literature Index
 040 Drug Dependence, Alcohol Abuse and Alcoholism
 LANGUAGE: German
 ENTRY DATE: Entered STN: 17 Jun 1999
 Last Updated on STN: 17 Jun 1999
 ED Entered STN: 17 Jun 1999
 Last Updated on STN: 17 Jun 1999

L99 ANSWER 38 OF 46 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95273034 EMBASE
 DOCUMENT NUMBER: 1995273034
 TITLE: Neurosteroids and GABA(A) receptor function.
 AUTHOR: Lambert J.J.; Belelli D.; Hill-Venning C.; Peters J.A.
 CORPORATE SOURCE: Department Pharmacology, Ninewells Hospital/Medical School, University of Dundee, Dundee DD1 9SY, United Kingdom
 SOURCE: Trends in Pharmacological Sciences, (1995) Vol. 16, No. 9, pp. 295-303.
 ISSN: 0165-6147 CODEN: TPHSDY
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 002 Physiology
 008 Neurology and Neurosurgery
 024 Anesthesiology
 029 Clinical Biochemistry
 050 Epilepsy
 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 10 Oct 1995
 Last Updated on STN: 10 Oct 1995
 ED Entered STN: 10 Oct 1995
 Last Updated on STN: 10 Oct 1995
 AB In 1994, a potent and selective interaction of the steroidal anaesthetic alphaxalone with the GABA(A) receptor was demonstrated. Subsequent studies established that certain naturally occurring steroids were potent positive allosteric modulators of the GABA(A) receptor. Although peripheral endocrine glands are an important endogenous source, the brain can synthesize 'neurosteroids', and these have the potential to influence

the activity of the GABA(A) receptor in the CNS. Systemic administration of steroids have clear behavioural effects. In this article, Jeremy Lambert and colleagues review recent advances in this field and discuss the therapeutic potential of this novel, non-genomic effect of steroids and investigate whether they may influence behaviour under physiological, or pathophysiological, conditions.

L99 ANSWER 39 OF 46 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:138635 BIOSIS
 DOCUMENT NUMBER: PREV200600141797
 TITLE: Correlations between REM sleep EEG spectral analysis and CSF GABA in clinically stable drug-free patients with schizophrenia: A pilot study.
 AUTHOR(S): Poulin, Julie [Reprint Author]; Van Kammen, Daniel P.; Kelley, Mary E.; Godbout, Roger; Neylan, Thomas C.; Nofzinger, Eric A.; Peters, Jeffrey L.; Tsai, Guochuan E.
 CORPORATE SOURCE: Univ Montreal, Ctr Rech Fernand Seguin, Montreal, PQ, Canada
 SOURCE: Neuropsychopharmacology, (DEC 2005) Vol. 30, No. Suppl. 1, pp. S247.
 Meeting Info.: 44th Annual Meeting of the American-College-Neuropsychopharmacology. Waikoloa, HI, USA. December 11 -15, 2005. Vanderbilt Univ Sch Med Dept Psychiat.
 CODEN: NEROEW. ISSN: 0893-133X.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; (Meeting Poster)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 22 Feb 2006
 Last Updated on STN: 22 Feb 2006
 ED Entered STN: 22 Feb 2006
 Last Updated on STN: 22 Feb 2006

L99 ANSWER 40 OF 46 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:215686 BIOSIS
 DOCUMENT NUMBER: PREV200100215686
 TITLE: Steroid modulation of GABAA receptors.
 AUTHOR(S): Lambert, J. J. [Reprint author]; Peters, J. A.; Harney, S. C.; Belelli, D.
 CORPORATE SOURCE: Department of Pharmacology and Neuroscience, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland, DD1 9SY, UK
 j.j.lambert@dundee.ac.uk
 SOURCE: Moehler, Hanns. Handbook of Experimental Pharmacology, (2001) pp. 117-140. Handbook of Experimental Pharmacology. Pharmacology of GABA and glycine neurotransmission. print. Publisher: Springer-Verlag GmbH and Co. KG, Heidelberger Platz 3, D-14197, Berlin, Germany; Springer-Verlag New York Inc., 175 Fifth Avenue, New York, NY, 10010-7858, USA.
 Series: Handbook of Experimental Pharmacology.
 ISSN: 0171-2004. ISBN: 3540676163 (cloth).
 DOCUMENT TYPE: Book
 Book; (Book Chapter)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 2 May 2001
 Last Updated on STN: 18 Feb 2002
 ED Entered STN: 2 May 2001

Last Updated on STN: 18 Feb 2002

L99 ANSWER 41 OF 46 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1989:345658 BIOSIS
 DOCUMENT NUMBER: PREV198937036755; BR37:36755
 TITLE: STEROIDAL MODULATION OF THE GABA-A-BENZODIAZEPINE RECEPTOR COMPLEX AN ELECTROPHYSIOLOGICAL INVESTIGATION.
 AUTHOR(S): LAMBERT J J [Reprint author]; PETERS J A
 CORPORATE SOURCE: NEUROSCI RES GROUP, DEP PHARMACOL AND CLIN PHARMACOL, UNIV DUNDEE, NINEWELLS HOSP AND MED SCH, DUNDEE DD1 9SY, SCOTLAND, UK
 SOURCE: Fidia Res. Found. Symp. Ser., (1989) pp. 139-156. BARNARD, E. A. AND E. COSTA (ED.). FIDIA RESEARCH FOUNDATION SYMPOSIUM SERIES, VOL. 1. ALLOSTERIC MODULATION OF AMINO ACID RECEPTORS: THERAPEUTIC IMPLICATIONS; LONDON, ENGLAND, UK, NOVEMBER 1987. XVIII+404P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS.
 Publisher: Series: FIDIA Research Foundation Symposium Series.
 CODEN: FRFSEL. ISSN: 1040-0451. ISBN: 0-88167-482-6.
 DOCUMENT TYPE: Book
 Conference; (Meeting)
 FILE SEGMENT: BR
 LANGUAGE: ENGLISH
 ENTRY DATE: Entered STN: 25 Jul 1989
 Last Updated on STN: 29 Jul 1989
 ED Entered STN: 25 Jul 1989
 Last Updated on STN: 29 Jul 1989

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 on STN

ACCESSION NUMBER: 2004-0136488 PASCAL
 COPYRIGHT NOTICE: Copyright .COPYRGT. 2004 INIST-CNRS. All rights reserved.
 TITLE (IN ENGLISH): Influence of hydroxypropyl methylcellulose polymer on in vitro and in vivo performance of controlled release tablets containing alprazolam
 AUTHOR: MAHAGUNA Vorapann; TALBERT Robert L.; PETERS Jay I.; ADAMS Sandra; REYNOLDS Thomas D.; LAM Francis Y. W.; WILLIAMS Robert O. III
 CORPORATE SOURCE: College of Pharmacy, Austin, TX, United States; Department of Pharmacology, The University of Texas-Health Science Center at San Antonio, San Antonio, TX, United States; Larkin Laboratory, The Dow Chemical Company, Midland, MI, United States
 SOURCE: European journal of pharmaceutics and biopharmaceutics, (2003), 56(3), 461-468, 29 refs.
 ISSN: 0939-6411
 DOCUMENT TYPE: Journal; (research paper)
 BIBLIOGRAPHIC LEVEL: Analytic
 COUNTRY: Netherlands
 LANGUAGE: English
 AVAILABILITY: INIST-17483, 354000114455910200
 UP 20040405
 AB The purpose of this study was to investigate the influence of hydroxypropyl methylcellulose (HPMC) molecular weight on pharmacokinetic and pharmacodynamic parameters of controlled release formulations containing alprazolam. Tablet formulations contained alprazolam, excipients, and either HPMC K4MP or HPMC K100L VP. A ten patient in vivo

clinical trial using a randomized, open-label, four-way crossover design was conducted in the fed and fasted states. Plasma alprazolam concentrations were determined for 72 h. The pharmacodynamic effects of alprazolam were monitored using subject rated sedation on visual analogue scale for wakefulness, observer rated sedation, and symbol digit modalities test (SDMT). Results indicated that the tablet formulations containing either HPMC K4MP or HPMC K100LVP had similar dissolution profiles, and the dissolution profiles did not change through 6 months at 40°C/75% RH or 12 months at 25°C/65% Relative Humidity (RH). The area under the plasma concentration-time curve, time to peak concentration, and peak plasma concentration were not significantly different between the two tablet formulations investigated in either the fed or fasted states. Pharmacodynamically, no significant differences in SDMT scores between the two formulations were found. In vitro dissolution results predicted in vivo pharmacokinetic and pharmacodynamic results irrespective of formulation or diet used in the controlled release tablet. The controlled release tablets were bioequivalent and pharmacodynamically equivalent irrespective of the tablet formulation.

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ACCESSION NUMBER: 2002-0395464 PASCAL

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TITLE (IN ENGLISH): Structure-based design of peptidomimetic antagonists of p56.sup.l.sup.c.sup.k SH2 domain

AUTHOR: HOBBS Christopher J.; BIT Rino A.; CANSFIELD Andrew D.; HARRIS Bill; HILL Christopher H.; HILYARD Katherine L.; KILFORD Ian R.; KITAS Eric; KROEHN Antonin; LOVELL Peter; POLE David; RUGMAN Paul; SHERBORNE Brad S.; SMITH Ian E. D.; VESEY David R.; WALMSLEY D. Lee; WHITTAKER David; WILLIAMS Glyn; WILSON Fiona; BANNER David; SURGENOR Allan; BORKAKOTI Neera

CORPORATE SOURCE: Roche Products Limited, 40 Broadwater Road, Welwyn Garden City, Hertfordshire AL7 3AY, United Kingdom; F. Hoffmann-La Roche Ltd, Pharma Division, Preclinical Research, Basel, Switzerland

SOURCE: Bioorganic & medicinal chemistry letters, (2002), 12(10), 1365-1369

ISSN: 0960-894X

DOCUMENT TYPE: Journal

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: United Kingdom

LANGUAGE: English

NOTE: 3/4 p. ref. et notes

AVAILABILITY: INIST-22446, 354000101241630100

UP 20020821

AB Starting from the tetrapeptide Ac-pYEEI-NHMe and using a structure-based approach, we have designed and synthesised a peptidomimetic ligand for p56.sup.l.sup.c.sup.k SH2 domain containing a conformationally restricted replacement for the two glutamate residues. We have explored replacements for the isoleucine residue in the pY + 3 pocket and thus identified 1-(R)-amino-3-(S)-indane-acetic acid as the most potent replacement. We also report the X-ray crystal structures of two of the antagonists.

L99 ANSWER 44 OF 46 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:61126 SCISEARCH

THE GENUINE ARTICLE: WC182

TITLE: Modulation of human recombinant GABA(A) receptors by pregnanediols
 AUTHOR: Belelli D (Reprint); Lambert J J; Peters J A;
 Gee K W; Lan N C
 CORPORATE SOURCE: UNIV DUNDEE, NINEWELLS HOSP & MED SCH, DEPT PHARMACOL & CLIN PHARMACOL, INST NEUROSCI, DUNDEE DD1 9SY, SCOTLAND; UNIV CALIF IRVINE, DEPT PHARMACOL, COLL MED, IRVINE, CA 92717; COCENSYS INC, IRVINE, CA 92718
 COUNTRY OF AUTHOR: SCOTLAND; USA
 SOURCE: NEUROPHARMACOLOGY, (1996) Vol. 35, No. 9-10, pp. 1223-1231

ISSN: 0028-3908.
 PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 28

ENTRY DATE: Entered STN: 1997
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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ED Entered STN: 1997
 Last Updated on STN: 1997

AB Utilising two point voltage-clamp techniques on *Xenopus laevis* oocytes expressing human ($\alpha(1)$ $\beta(1)$ $\gamma(2L)$) recombinant GABA(A) receptors, the GABA modulatory actions of six naturally occurring neurosteroids have been determined and compared with those of known positive allosteric modulators. The anaesthetic steroids 5 α - and 5 β -pregnan-3 α -ol-20-one produced a concentration-dependent enhancement of the GABA-evoked current. The maximal enhancement of the agonist-induced response produced by these steroids was intermediate between that of pentobarbitone and diazepam, but much greater than that caused by bretazenil. For both the 5 α and 5 β steroid a reduction of the 20 ketone group to form either the corresponding 20 α or 20 β hydroxy steroid produced, in all cases, a reduction in potency and a decrease in the maximal effect. The relationship of steroid structure to these two parameters is considered. The influence of the α or subtype ($\alpha(x)$ $\beta(1)$ $\gamma(2L)$, where $x = 1, 2$ or 3) for the behaviourally active 5 α -pregnan-3 α , 20 α -diol is also determined. Although the maximal effect of the steroid is not influenced by the α subtype, the $\alpha(2)$ -containing receptor exhibits a modest decrease (approximately 6-fold) in potency compared to $\alpha(1)$ - and $\alpha(3)$ -containing receptors. The results described here are discussed in relation to the distinct behavioural actions of the neurosteroids. Copyright (C) 1996 Elsevier Science Ltd

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ACCESSION NUMBER: 1993:495200 SCISEARCH

THE GENUINE ARTICLE: LQ960

TITLE: REACTIONS OF HYDROXYGLYCINES - NEW SYNTHETIC ROUTES TO 4-PHENYLQUINAZOLINE DERIVATIVES

AUTHOR: HOEFNAGEL A J (Reprint); VANKONINGSVELD H; VANMEURS F; PETERS J A; SINNEMA A; VANBEKKUM H

CORPORATE SOURCE: DELFT UNIV TECHNOL, ORGAN CHEM & CATALYSIS LAB, JULIANALAAN 136, 2628 BL DELFT, NETHERLANDS (Reprint); DELFT INSTRUMENTS XRAY DIFFRACT BV, 2624 BD DELFT, NETHERLANDS

COUNTRY OF AUTHOR: NETHERLANDS
 SOURCE: TETRAHEDRON, (30 JUL 1993) Vol. 49, No. 31, pp. 6899-6912.

PUBLISHER: ISSN: 0040-4020.
 PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD
 LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; LIFE

LANGUAGE: English

REFERENCE COUNT: 23

ENTRY DATE: Entered STN: 1994

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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ED Entered STN: 1994

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AB Reaction of hydroxyglycine with 2-aminobenzophenones gives 1,2-dihydro-4-phenyl-quinazoline-2-carboxylic acids in high yields and under mild conditions. These can be smoothly converted into the corresponding 3,4-dihydro isomers and into quinazoline derivatives via rearrangement and oxidation by air, respectively. The X-ray crystallographic structure of 6-chloro-1,2-dihydro-1-methyl-4-phenylquinazoline-2-carboxylic acid shows the carboxylate group at C(2) and the methyl group at N(1) to be in axial positions.

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ACCESSION NUMBER: 1992:400608 SCISEARCH

THE GENUINE ARTICLE: JB761

TITLE: THE ACTIONS OF ENDOGENOUS AND SYNTHETIC PREGNANE STEROIDS ON GABA(A) RECEPTORS

AUTHOR: HILLVENNING C (Reprint); LAMBERT J J; PETERS J A ; HALES T G; GILL C; CALLACHAN H; STURGEON N C

CORPORATE SOURCE: UNIV.DUNDEE, NINEWELLS HOSP & MED SCH, DEPT PHARMACOL & CLIN PHARMACOL, NEUROSCI RES GRP, DUNDEE DD1 9SY, SCOTLAND (Reprint); UNIV CALIF LOS ANGELES, CTR HLTH SCI, SCH MED, DEPT ANESTHESIOL, LOS ANGELES, CA 90024; ICI PHARMACEUT PLC, BIOSCI 2, MACCLESFIELD SK10 4TG, CHESHIRE, ENGLAND

COUNTRY OF AUTHOR: SCOTLAND; USA; ENGLAND

SOURCE: ADVANCES IN BIOCHEMICAL PSYCHOPHARMACOLOGY, (1992) Vol. 47, pp. 93-102.

ISSN: 0065-2229.

PUBLISHER: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.

DOCUMENT TYPE: General Review; Journal

LANGUAGE: English

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